THE STUDY OF HEREDITY

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THE STUDY OF HEREDITY

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TO

PROFESSOR E. S. GOODRICH, F.R.S.

PREFACE

DURING the present century a vast amount of information has been accumulated on the subject of heredity. This mass of material has, however, by no means obscured the general principles which underlie hereditary transmission and the control of variation. On the contrary, it has served to demonstrate their application even in situations of the greatest superficial complexity. But the fundamental laws of heredity are not complex, nor are many of the far-reaching deductions which can be drawn from them. Indeed, anyone who can spare a few leisure hours for study may readily master their working, so as to apply them and to appreciate their significance.

This is a labour worth attempting. Not only are these laws very simple, but they are of extremely wide application—alike in animals and plants. All those who derive pleasure, or even profit, from the study of living things, will find an added interest in knowing how their variation is controlled, how they

evolve, or how desirable qualities may be established in the stocks which they may possess. Nor must it be forgotten that these same laws apply to the human race. A knowledge of them is becoming essential for the student of a variety of social problems, and for those who advocate, or even oppose, eugenic reform. It has been found that numerous diseases, or the tendencies to acquire them, are inherited ; so also, it has been proved, are many normal characteristics, mental as well as physical : medical men and educationists must certainly be acquainted with the principles upon which these facts depend.

There must be many who have no previous knowledge of biology and yet feel that the study of heredity may have something to offer them. I have endeavoured to arrange this book to meet their needs. It might have been possible to write it with the use of exceedingly few scientific terms. I have not attempted such a *tour de force*. Not only would it involve much circumlocution, but it would reduce the usefulness of the work very considerably. One of the objects of this Series is to place students in a position to extend their information by further reading. For this they would be ill equipped had

they not been introduced to certain technical words a knowledge of which will be presumed by the authors they may require to consult. However, I have explained each one the first time that it is used, and provided a glossary in which I have defined all of them. Consequently, no initial knowledge of science is required in order to follow the account which is given here.

I am indebted, as so often in the past, to Professor Julian Huxley and to Professor E. S. Goodrich for helpful advice and criticism. Their valuable suggestions have been of the greatest assistance to me in the preparation of this book. I am most grateful to Dr. G. R. de Beer for his kindness in reading the proofs. I should like to express my thanks to Messrs. Methuen & Co., Ltd., for kindly allowing me to reproduce Figs. 3 and 4 from my *Mendelism and Evolution*.

E. B. F.

OXFORD,
January 1938.

CHAPTER I

INTRODUCTION : THE PHYSICAL BASIS OF HEREDITY

IT is impossible to begin the study of heredity without some slight knowledge of the structure of living organisms and, in particular, of the means by which the hereditary material is passed on from one generation to another. Although I have endeavoured to write this book in such a way as to require the minimum of information on these subjects, references to certain aspects of them cannot be avoided. I shall therefore devote this short introductory chapter to giving a brief account of the physical basis of heredity, in so far as it is necessary to make the remainder of the work easily intelligible.

The living substance of the body, whether of plants or of animals, is called *protoplasm*. It is normally divided up into a vast number of microscopical units, known as *cells*, each of which is specially fitted for the particular function which it has to perform. For the different parts of all organisms, except the

smallest and simplest, are adapted to a variety of purposes, and are composed of cells modified in appropriate ways : whether it be for transmitting messages, for manufacturing substances required by the body, for contraction (and so bringing about movement), or for many other duties. Now the activities of each cell are controlled by a highly organized region, the *nucleus*, which is enclosed within a membrane. This shuts it off from the remainder of the protoplasm, to which the name *cytoplasm* is given.

In the majority of animals and plants, two individuals co-operate in order to reproduce themselves. For this purpose special cells are set apart. These are called *gametes*. They can be liberated from the body, and two of them fuse to form the first cell of the new individual. Now it is usual to find that some division of labour is adopted in this process, the gametes being of two distinct types. Of these, one is relatively large and passive, containing much food material stored in its cytoplasm for use during early development. This is the egg. The other is, by comparison, minute, its small size being produced wholly by a reduction in the amount of its cytoplasm. This makes it possible for it to be carried some distance,

by its own activity or by external agencies, until it can reach and fuse with, or fertilize, the egg. In most animals it is itself capable of active movement, and is called a spermatozoon. In plants, on the other hand, it is usually enclosed in the pollen-grains, which can be carried about by the wind, by insects, or by other means. Thus, most organisms are differentiated into two types: the female sex producing the quiescent gametes, and the male sex producing those capable of dispersal.

It is important to notice that, as living organisms are derived from each other, there is a *continuity* of living substance, carried by the gametes, from generation to generation. Therefore, the fundamental resemblance of the offspring to its parents is due to the fact that it starts from the same material which, growing under similar conditions, attains a similar end.

When an animal or plant grows, it does so rather by a multiplication of its cells than by an enlargement in their size. Those first formed are not adapted to particular purposes, for all the various types have to be derived from them. As growth proceeds, however, they become gradually modified in different directions to perform special functions. This

modification principally affects the cytoplasm: the nucleus remains essentially unchanged, its constancy being indicated by a most important feature of its organization. For every nucleus contains certain structures called *chromosomes*, and normally their number is the same in every cell of the body and in every individual of the species. Now it will be appreciated that fertilization is an additive process. Two cells combine to form one, the first of the new individual: yet the number of chromosomes remains constant in every generation. This is due to the fact that the gametes contain half the normal number of chromosomes only. Consequently, half of them in each individual are derived from one parent and half from the other: for they are self-perpetuating bodies. If, owing to some accident, one of them is lost, the organism cannot manufacture it anew.

It will now be realized that an essential feature both of growth and reproduction is the division of the cells. That of their cytoplasm calls for no detailed comment. The nucleus first divides. The cell then becomes hour-glass shaped and subsequently breaks across at the constriction, so separating into two parts; the process occurring with no special mechanism for ensuring an accurate

distribution of the cytoplasm between them. Not so with the nucleus : the perpetuation of the chromosome number indicates that its division must be accomplished with exactitude, and it is essential that we should briefly consider how this is achieved.

At the outset, however, it must be mentioned that the chromosomes are not always visible. They can only be distinguished when the cell is dividing, for at that time a substance (' chromatin '), which easily takes up certain dyes, becomes precipitated upon them, showing up their structure. At other times the chromatin floats away from them as scattered granules, leaving the chromosomes invisible. We know, however, that they persist in some form from one nuclear division to another.

The first sign, then, that a cell is going to divide is given by the reappearance in its nucleus of the chromosomes, in a form in which they can be artificially stained. Each one of them is already longitudinally split into two parts (in preparation of the ensuing division), which at this stage are held closely together by an attraction between them. Moreover, the chromosomes themselves are present in pairs. Where, as often, they differ in size or shape, two of every kind can

be distinguished. These pairs constitute what are called *homologous chromosomes*, and their members are derived respectively from the two parents.

When they first appear the chromosomes take the form of long thin threads. They are quite separate from one another, but easily damaged in such a way that their ends run together to produce a continuous coil. Gradually they shorten and thicken into rods, and the membrane surrounding the nucleus disappears, so that its contents lie freely in the cytoplasm. Meanwhile, some of the protoplasm forms a spindle-shaped body enclosing the chromosomes. They take up a position in the centre of this structure, where it is widest. The two parts into which each chromosome has been longitudinally split at last separate from one another and pass in opposite directions to the tips of the spindle. Here, therefore, they collect into two groups, each containing a longitudinal half of every chromosome. The spindle then disappears, a new nuclear membrane forms round each group, and the cell divides between them. The chromosomes gradually become invisible and, before the next division, have doubled in thickness, so that each of the two new nuclei exactly resembles the single

one from which it was derived. This process is called *mitosis*. It is the one normally adopted by all cells when they divide. An exception is, however, to be found in the *germ-cells*, which are those giving rise to the gametes. For at the end of their development a special mechanism reduces the number of their chromosomes to half.

The need for such an occurrence has already been pointed out, and it is necessary to explain very briefly the chief features of it. However, it must be understood that it involves a number of complex and important phenomena upon which we can hardly touch here, and all those not immediately relevant to our purpose must be omitted.

In general terms, it may be said that after the germ-cells have passed through a series of ordinary mitoses, their chromosomes divide once while their nuclei divide twice. These are the last two divisions which they undergo and, naturally, they produce cells having only half the normal number of chromosomes. But this halving is not a random process, for each contains one member of every homologous pair. The double sets are of course restored when fertilization takes place.

In addition to chromosome reduction, this process subserves a second and entirely

different purpose. It allows sections of material to be exchanged between the pairs of homologous chromosomes before their separation. However, when this occurs, they have already split longitudinally in preparation for the ensuing division : consequently the interchange involves not *whole* chromosomes, but one of the two halves into which each has divided. Successive exchanges down the length of a pair may involve sometimes one, sometimes another of their longitudinal halves. They do not, however, affect both parts at the same time. To make the point clearer, we may say that, at the moment we are considering, the homologous chromosomes consist of four units. These are the two members of each pair, themselves each longitudinally divided into two. Let us call these *A* and *B*, representing the two parts into which one chromosome has divided, and *M* and *N*, representing the products of division of the other. At one level, *A* may exchange material with *M* for a certain distance while *B* and *N* preserve their integrity, at another the interchanging pairs may be *B* and *M*, and at a third *B* and *N*. The significance of this occurrence will be discussed in subsequent chapters.

Here then we have before us the two

features which distinguish the division of the germ-cells at the end of their development. First, that the number of their chromosomes is halved, every cell receiving one member of each homologous pair. Secondly, an interchange of blocks of material takes place between homologous chromosomes after they have divided longitudinally into two. This exchange involves only one of the products of their division at each level along the chromosomes.

The facts so far stated provide all that is required for understanding the account presented in this book. It seems probable, however, that some readers may wish to know something of the way in which these two results are attained. For their convenience, I shall give a brief account of the mechanism which achieves them. It is suggested that all those who have made no previous study of biology should read at least to the end of Chapter V, or the remainder of the book, before returning to complete the present section. It contains a summary of this aspect of cell-division which I believe is hardly accessible elsewhere in so brief a form. Anyone who desires a more extended account of it should consult the works of White and Darlington included in the bibliography

(p. 251). The technical terms which are employed for the first time in the remainder of this chapter are not included in the glossary, as they will not be required subsequently.

The process which brings about an exchange of material between homologous chromosomes, and distributes one member only of each to every gamete, is called *meiosis*. As already mentioned, it occupies the last two divisions of the germ-cells. The first sign of its occurrence is of course given by the appearance of the chromosomes in the nuclei. But the division is a precocious one; it takes place before the chromosomes are ready for it, so that they have not yet split longitudinally into two parts, as they have time to do before an ordinary mitosis.

It is important to notice that in the early stage of almost all cell-divisions, an attraction between identical units brings the material of the chromosomes together *in pairs*. Normally, as we have seen, this holds in close association the longitudinal halves of each chromosome, which are called *chromatids*. Since, however, the chromosomes have not yet so divided at the start of meiosis, this same attraction draws together *whole chromo-*

somes : these will evidently be the homologous pairs, for it is in them that identical material is to be found. Consequently, at an early stage the chromosomes begin to associate together two by two, those which do so being of similar size or shape.

The chromosomes are spirally coiled, and at first they are long and thin, as long as the diameter of the nucleus or longer, being stretched out by surface tension. Gradually this is relaxed as they lose water and shorten : consequently their spirals tend to become closer. What now happens can be made clear by a simple analogy. Suppose we take two thick strands of worsted. Each is spirally coiled. By pulling them out with the fingers, starting first in the middle of each, they may be stretched in such a way as to leave their ends free to turn. Now, still keeping them stretched, bring them side by side, and then allow the tension to relax. The surface of the threads is ' sticky,' in the sense that one cannot slide freely over the other. Consequently, as they shorten, the increasing twist is taken up not by each individual thread but by the pair as a whole. It will be found, therefore, that they wrap round one another.

So with the chromosomes : they too are

under tension and are spirally coiled, they too come together in pairs, and they are in the same sense ' sticky '—they are not free to slide freely one over the other. Thus, as the tension is relaxed and the pairs shorten, they coil not individually but as a pair : wrapping round one another, as do threads in the process of spinning. They have, however, sufficient rigidity to prevent the twist from forming a very close spiral.

All this takes time to accomplish and, some while after it is completed, the chromosomes reach the stage (attained in mitosis before they appear) when each splits longitudinally into two chromatids. The attraction of individual units *in pairs* still persists, but now it is satisfied (as in mitosis) as an association of pairs of *chromatids* instead of whole chromosomes : for the homologous pairs now consist of four parts, the two chromosomes each split longitudinally into two chromatids. Therefore the pairs of chromosomes fall apart, their twist being taken up by the pairs of chromatids into which each has divided. It is now seen that an astonishing thing has happened. Sections of material have been interchanged between the pairs of chromatids derived from different chromosomes. Such an interchange involves two pairs only in any

one region. The points of exchange are determined by the points of contact established when the chromosomes wrap round one another as they contract. We have then in the nucleus a number of sets of chromatids, four in each. *A* and *B* (let us say) derived from one chromosome, *M* and *N* from another. At intervals *A* or *B* has exchanged

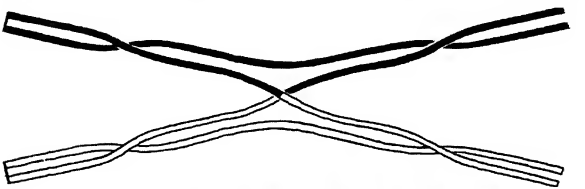

FIG. 1.—Two of the chromatids derived from the longitudinal splitting of different, but homologous, chromosomes have exchanged material. Since they have not exchanged partners, a *chiasma* has formed, where they cross over one another in the form of an X.

materials with *M* or *N*. However, they do not exchange partners. The two chromatids derived from each chromosome always lie side by side. Evidently, therefore, two of the four chromatids must cross over in the form of an X at each point where material is transferred (Fig. 1.). Such crosses are called *chiasmata*, and the existence of one or more of them serves to keep in association the pairs of homologous chromosomes (composed of

two chromatids each) until the time comes for nuclear division, so that they may separate from one another in a regular manner.

In this fashion, therefore, is achieved the interchange of material, actually between *chromatids* derived from homologous chromosomes, which is one of the two fundamental processes attained by meiosis. It will be seen that it is brought about by simple mechanical means, and that it depends primarily upon the precocious nature of the division in which it takes place, for it occurs before the chromosomes have split into chromatids.

We must now consider the other function of meiosis, that of chromosome reduction. The phenomena which we have just described take place during the time that the cell is preparing itself for its penultimate nuclear division. When the time for this arrives, the members of the homologous chromosomes separate from one another, whole chromosomes migrating in opposite directions towards opposite ends of the spindle, which has been formed as in mitosis. Now these whole chromosomes are, as explained, already split longitudinally—one would have thought for this, the ensuing division. Yet the two chromatids composing

each of them do not separate, but pass together as a single chromosome along the spindle. Thus it will be seen that two groups of chromosomes collect at its ends, each consisting of one member of every homologous pair split into a pair of chromatids.

A word of explanation is required here. Why do the chromatids not part from one another in the usual way? It has been seen that their formation took place relatively late, because the division began early, and it appears that the separation of each chromosome into two parts is not quite complete even when they are due to move apart. The pairs of chromatids are still united at one point (the 'attachment constriction') and must consequently migrate together as whole chromosomes. At this time then, homologous regions have to be pulled apart at those levels where sections have been interchanged. We can see that they resist this, for the arms of the chiasmata become drawn out and tense before the attraction can be overcome.

The first of the two meiotic divisions thus ends with the formation of two new cells both possessing one chromosome of every type. Each of these is divided into two chromatids, some of whose sections contain

material interchanged from those composing their homologous chromosome, which is now in another nucleus.

Then follows the final division of the germ-cells. The two chromatids forming each chromosome at last separate and pass respectively into the groups which will form the new nuclei. As after a mitosis, they grow until they have doubled their thickness. Thus they become the chromosomes of the cells which will develop into gametes, which therefore contain half the normal number, one from every homologous pair. Both functions of meiosis have then been accomplished.

In summarizing the effects of this process, we should notice in particular that it brings about a separation of homologous material. It will be recalled that the bodies reaching the two ends of the spindle in an ordinary mitosis include a portion (actually a longitudinal half) of every chromosome possessed by the organism. However, the products of only one member of every homologous pair reach each gamete. If no interchange of material had taken place, this separation would be accomplished wholly at the first meiotic division. The second meiotic division would then, as in a mitosis, provide the two cells

which it produces with substance from every chromosome contained by that which gave rise to them. In reality, however, the separation of homologous material is achieved alternately at the first and second meiotic division as we pass from one interchanged segment to the next down the lengths of the chromosomes. Meiosis, then, requires two cell divisions for its fulfilment.

The description of cell division given here will be found to differ considerably from accounts written ten or fifteen years ago, for recent researches have served to alter and to clarify our concepts of this process very considerably. The author would here like to pay a tribute to the work of Dr. C. D. Darlington, to whose technical skill and theoretical analysis these advances are so largely due.

CHAPTER II

THE LAWS OF INHERITANCE

THE development of all living things and of their distinctive characteristics is controlled both by heredity and by the environment. We are all aware that two individuals brought up in different surroundings, or exposed to different treatment, will themselves come to differ, however much they may originally have resembled one another. On the other hand, identity of conditions will tend to uniformity only within certain limits, and to a degree which is greatest in those forms which we judge most nearly related. This in itself indicates the operation of organic inheritance, the existence of which can, in fact, be established by a general proof, quite apart from those instances which are suitable for direct experiment (pp. 99–100). It will here be most convenient first to study heredity, and subsequently to consider how its effects may be modified by the environment.

The characters of organisms are under the

control of pairs of factors the members of which are derived respectively from the two parents, one being carried in each gamete. The corresponding pairs are called *allelomorphs*, and the individual factors which comprise them are known as *genes*. In reality, the genes have numerous effects, so that they determine the development of sets of characters. The transmission of the genes can be followed by studying the fate of the various characters which they control. In practice, however, it is convenient to select from among these any one which can easily be examined, and use it to mark the presence of the gene whose inheritance we wish to follow. We shall adopt this procedure here, and return in Chapter VI to discuss the implications of the fact that the effects of the genes are, in reality, multiple.

The pairs of factors forming the allelomorphs are called *homozygous* if they are identical, and *heterozygous* if they differ from one another. Their capacity to assume a number of different states (*multiple allelomorphs*) allows the occurrence of variations in the characters which they govern. These tend to be of a contrasted type for they affect a given

not more than two of the possible alternatives can coexist in any one individual (for exceptions to this statement, see pp. 94–7).

With these facts in mind, we may trace the fate of a pair of contrasted characters when we cross individuals exhibiting them. From it we can deduce the manner in which the genes controlling them have been transmitted. In poultry, the Andalusian breed has several colour varieties. If we cross a black bird with a white, all the offspring are grey. They are, therefore, intermediate in appearance, though called 'blue' by poultry fanciers. These are the 'first filial' generation of our cross (denoted F_1: the original birds forming the parental, or P_1, generation). If we mate the grey F_1 birds with one another, we obtain a 'second filial generation' (F_2), comprising the inbred grandchildren of our first cross. This too contains intermediate birds, but the original black and white types reappear in addition. Evidently, then, the second filial generation is more variable than the first: in this instance, it contains three colour forms instead of one. Now it is important to notice that these appear in a constant proportion, the blacks and whites being in equal numbers, and the greys twice as

numerous as either of them: a ratio of 1 : 2 : 1.

It is worth while to reflect on these facts. First, they tell us that the genes have throughout retained their identity. Though the *characters* for which they are responsible blended, the genes did not do so, for we recover them in a proportion of the F_2 offspring, and we can prove them uncontaminated. For, if we interbreed two of the F_2 blacks, or two of the whites, we can found black or white strains which will remain pure. Since the F_1 generation is intermediate, and since the number of blacks and whites is equal in F_2, the parents contribute equally to the heredity of their offspring: it makes no difference whether it is the cock or the hen which is black. Consequently, a colour-determining gene from each P_1 parent must have reached the offspring, whose grey plumage was therefore the result of a pair of factors, black- and white-determining, acting together to produce an intermediate effect. These, as we see, remained distinct, and must have parted from one another to enter different germ-cells, which would each contain one member only of this particular pair of genes. It is evident that this is so: for such a situation will

lead to the production of white-determining and black-determining gametes in equal numbers by every F_1 individual. The chances, then, are equal that at mating, each gamete will fuse with its own, or with the other, type. Consequently these will form both black or grey and white or grey birds all in equal numbers, so producing one black, two grey, and one white out of every four: just as when we toss together two coins, our throws on the average result in both obverse, mixed, and both reverse, in a 1:2:1 ratio. We must notice that gametes have an equal chance of fusing whether the allelomorphs they contain are similar or dissimilar. The grey group could not form half the total unless this were so.

Thus we see that the black birds, as the white, are produced by a pair of similar genes, black- or white-determining: that is, they are homozygous. Clearly, when two black or two whites are mated they will breed true, for only identical factors separate from one another into different germ-cells. The grey birds, however, are heterozygous, being the product of black-determining and white-determining factors jointly. Evidently they can never breed true.

Our results then lead us naturally to

certain conclusions. The genes controlling the characters are present in pairs (allelomorphs). The members of the pairs separate from one another during the formation of the gametes, which contain one member only of each. They recombine at random to form pairs again at fertilization, but the genes retain their identity, ready to separate once more when gametes are produced by the new generation.

Two essential conclusions are to be drawn from this simple analysis: that the members of the allelomorphs do not blend, and that they separate from one another, or *segregate*, at the formation of gametes, which receive one member only of each pair. These constitute the first of the two fundamental laws of heredity, the *law of segregation*, which were discovered by Father Gregor Mendel. He had experimented on inheritance in edible peas, and to his ability we owe the inception of the theory of particulate inheritance, in which the hereditary units remain distinct, as opposed to a blending mechanism by which they merge and lose their identity.

It will already have become apparent to the reader that there exist vehicles perfectly suited to the distribution of the genes,

and that these are the chromosomes. They had not been discovered when Mendel worked in the middle of last century, and he could only deduce such a system as they provide. Now, however, it is clear how well they are adapted to convey the hereditary units. The chromosomes are present in pairs (homologous chromosomes) in the body-cells. So are the genes, whose pairs are the allelomorphs. The two members of each chromosome pair separate from one another in the germ-cells, one passing to each gamete. At this time segregation occurs when the pairs of genes also separate, each gamete receiving one only of the partners. The additive nature of fertilization, when the pairs of homologous chromosomes are restored, exactly parellels the restoration of the allelomorphs which ensures a recombination of the genes. The conclusion that the chromosomes carry the genes already seems inevitable : it is, however, susceptible of complete proof (pp. 47, 49–50, 90–5).

It will be realized that, in studying segregation, we have in reality to deal with this process at three different levels. The separation, or segregation, from one another of the members of the homologous chromosome pairs during the formation of the germ-

cells, results in the segregation of the genes which they carry. This, in its turn, brings about visible segregation in the characters which the genes control. We may now consider some further applications, and superficial modifications, of these principles.

In the instance which we discussed, it will be recalled that we mated two heterozygous birds (grey in colour) to produce an F_2 generation segregating in a 1 : 2 : 1 ratio. Let us investigate the result of mating together a heterozygote (in this instance a grey bird) and a homozygote (either black or white) : it will be valuable to study such a cross in relation to the chromosome basis of heredity.

The grey birds possess in every cell of the body a pair of allelomorphic genes controlling plumage-colour. This pair is heterozygous, one member being black-determining and the other white-determining. In the black (to select one of the two possible types) this allelomorphic pair is homozygous, both genes determining black coloration. Consequently, half the gametes of the grey bird will receive a black- and half a white-determining gene. But the gametes of the black bird will all contain a gene for the production of black plumage. When these

are fertilized by gametes from the grey bird, the chances are equal that they may meet with another black determinant, so producing a black bird, or with a white determinant, producing a heterozygous grey one. Black and grey birds therefore appear in a 1 : 1 ratio. Any mating such as this, between a heterozygote and a homozygote, is called a '*back-cross*,' since one way in which it can arise is to cross the heterozygous F_1 generation back to one of the homozygous P_1 parents. The offspring from a back-cross form what is known as an R_2 generation, and they will always segregate in equal numbers.

It is usual to find that the heterozygote is not intermediate between the two homozygous types, but that one of them partly or wholly obscures the other when the genes controlling them are present together. The character which manifests itself in these circumstances we call *dominant*, and that which is obscured we call *recessive*. Evidently the existence of dominance will serve to mask the segregation of the heterozygotes, which will be scored with that homozygous class which they resemble. Thus the 1 : 2 : 1 ratio of the F_2 generation will become a 3 : 1 ratio. That the larger of the two classes it

then contains is really composed of homozygotes and heterozygotes in a ratio of 1 : 2 may be proved by making further crosses. It can be shown that one-third of them breed true and two-thirds do not. We will take an example of this condition.

If we mate a pure-bred rabbit of the normal brown coloration with one of the well-known albino type, having white fur and pink eyes, all the (F_1) offspring will be normal in appearance. When we interbreed them, their progeny will include both normals and albinos in a 3 : 1 ratio. Thus it appears that normal coloration is dominant and that the albino type is recessive. If a number of the normal brown individuals of the F_2 generation be mated with albinos, we shall find that one-third of them produce normal offspring only. They were the homozygous normals. Two thirds, on the other hand, will produce both normals and albinos in equality. This is evidently a ' back-cross ', and these normals were heterozygotes. Our 3 : 1 ratio is in reality a ratio of 1 : 2 : 1 obscured by dominance.

These facts can be explained diagrammatically. For this purpose it is usual to indicate the genes composing a pair of allelomorphs by similar letters, using the

capital for that determining the dominant character. We may therefore represent the above cross as follows. In the homozygous condition, brown colour is produced by an allelomorphic pair *AA*, whose members are carried in a pair of homologous chromosomes. In the albino, these genes are in their alternative phase, *aa*. The members of each pair will segregate in the separating chromosomes during the formation of gametes. Those produced by the homozygous dominant will therefore each contain one gene *A*; similarly, those produced by the recessive will each contain one gene *a*. These will combine to produce heterozygotes of the constitution *Aa*: the pairs of allelomorphs have now been restored. These F_1 individuals will themselves produce two types of gametes in equal numbers, carrying *A* or *a*. They can combine in four different ways in the F_2 offspring, as illustrated in Fig. 2.

We have so far considered the inheritance only of pairs of genes when treated as isolated units. Mendel himself had examined the relation of two or more pairs when studied simultaneously. He summarized his views on this subject in the second of his two principles, the *law of*

independent assortment. This asserts that the segregation of any one pair of allelomorphs is independent of the segregation of any other pair. Granting the truth of this contention, the behaviour of any number of pairs of genes may be predicted. Thus

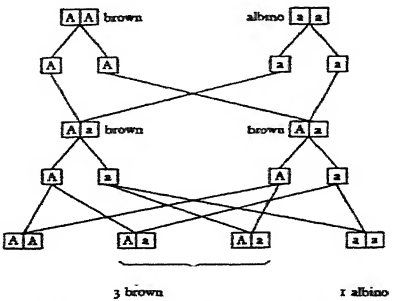

FIG. 2.—Segregation in the second hybrid generation (F_2) of a cross between two contrasted characters: brown (dominant) and white coat-colour in the rabbit.

if two sets of characters each segregate in a 3 : 1 ratio in the F_2 generation, they will, when taken together, segregate in a combination of two such ratios; that is to say, in a ratio of 9 : 3 : 3 : 1. Similarly, a back-cross involving two pairs of allelomorphs will lead to the production of four classes in the R_2 generation, all, of course, appearing in equal numbers. These facts become per-

fectly intelligible when illustrated by an example.

There is a small shrimp-like animal, *Gammarus chevreuxi*, which has been much used in the study of inheritance. In the Crustacea, the group to which it belongs, the surface of the eyes is divided into a number of 'facets', each representing the upper end of a distinct light-perceiving organ. One pair of allelomorphs controls the colour of these facets, which may be black or red, the former being dominant. A second pair determines whether or not they shall be separated from one another by white pigment. The condition with the white 'inter-facetary' pigment is the dominant one. The double dominant state (with black facets and white pigment between them) is that normally found. If a pure-bred individual of this type is crossed with one having red facets and no white pigment, the F_1 generation will evidently exhibit both dominant characters: all the animals comprising it having black facets, with white pigment between them. When we interbreed these 'double heterozygotes', we shall raise an F_2 generation in which each character will segregate in a 3 : 1 ratio, independently according to Mendel's second law. That

is to say, four types will now appear : black-with-white, black-no-white, red-with-white, red-no-white, in a 9 : 3 : 3 : 1 ratio. In the back-cross, obtained by mating the F_1 individuals to the homozygous recessives having red-no-white eyes, the same four types will appear, but in equality.

These facts may also be explained diagrammatically. For this purpose we shall employ different letters for the two pairs of allelomorphs using, as before, the capital for that determining the dominant character in each, as follows. In the homozygous condition, black facets are produced by an allelomorphic pair *RR* carried in one pair of homologous chromosomes, and the presence of white interfacetary pigment by a second allelomorphic pair *WW* carried in another. The corresponding genes in the red-no-white form are, respectively, *rr* (red facet production) and *ww* (inhibition of white pigment). The members of each pair of allelomorphs segregate at the formation of the gametes : every one produced by the double dominant will therefore contain the factors *R* and *W*, similarly all those produced by the double recessive will all contain *r* and *w*. They will combine to produce heterozygotes of the constitution *RrWw*.

These F_1 individuals will themselves produce gametes of four types in equal numbers for the chances are equal that *R* may pass to a gamete with *W* or with *w*; so with

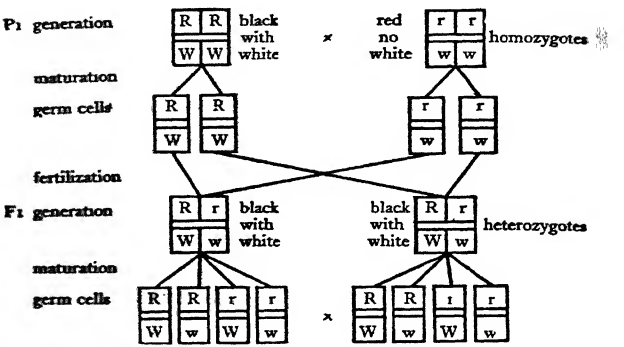

FIG. 3.—Diagram illustrating the formation of four types of germ cells by the individuals of the F_1 generation of a cross involving two pairs of independently assorting factors. These are: black, dominant to red, facet-colour, and the presence of white inter-facetary pigment, dominant to its absence, in the eyes of *Gammarus chevreuxi*. The factors in different chromosome-pairs are separated by a double line, those in homologous chromosomes (the two members of the same chromosome-pair) by a single line.

the equally numerous *r* genes, which also may be included with *W* or *w*, giving the assortments R*W*, R*w*, *r*W, and *rw*, all in equal numbers.

These facts are illustrated in Fig. 3. The

four different kinds of gametes produced by each F_1 individual can combine in sixteen

F_1 germ cells	RW	Rw	rW	rw
RW	**RRWW** black with white	**RRWw** black with white	**RrWW** black with white	**RrWw** black with white
Rw	**RRWw** black with white	**RRww** black no white	**RrWw** black with white	**Rrww** black no white
rW	**RrWW** black with white	**RrWw** black with white	**rrWW** red with white	**rrWw** red with white
rw	**RrWw** black with white	**Rrww** black no white	**rrWw** red with white	**rrww** red no white

F_2 generation = 9 black with white, 3 black no white, 3 red with white, 1 red no white.

FIG. 4.—Recombination at fertilization of the F_1 germ cells, whose formation is illustrated in Fig. 3. They produce an F_2 generation in which four types appear, segregating in a 9 : 3 : 3 : 1 ratio.

different ways in the F_2 offspring, as represented in Fig. 4. It will be noticed that these combinations give rise only to nine

separate types [1] and, owing to the existence of dominance, only to four visibly distinct classes. The double recessives, (red-no-white, *rrww*) can of course give rise to but one kind of gamete, *rw*. This, when mated with the double heterozygote (*RrWw*, producing four kinds of gametes in equal numbers), will result in an R_2 generation segregating in equality, as illustrated in the lowest horizontal line of the table in Fig. 4.

It will be seen that the independent assortment of the genes allows a reshuffling of the characters to take place. This is an important fact. It enables desirable qualities present in different individuals to be combined, so long as they are controlled by different pairs of allelomorphs. Another point of some practical significance emerges from the instance which we have discussed. Only four out of the sixteen combinations provide pure-breeding (homozygous) types, and these include one of each of the visibly distinct classes. Of these the recessives will always breed true, but the behaviour of the dominants in this respect is uncertain.

A little reflection will show that in reality

[1] These are *RRWW*, *RRww*, *RrWW*, *RRWw*, *RrWw*, *rrWw*, *Rrww*, *rrWW*, *rrww*, in a ratio of 1 : 1 : 2 : 2 : 4 : 2 : 2 : 1 : 1.

the law of independent assortment cannot be universally applicable. Only those allelomorphs which are situated in different pairs of chromosomes can segregate independently : a fact which could hardly have been predicted theoretically in advance of the discovery of the chromosomes, and Mendel himself did not chance to light upon an instance in which his second law is invalid. However, the number of chromosomes rarely exceeds a few dozen pairs, and is often quite small. Man has twenty-four pairs, and a fruit-fly, *Drosophila melanogaster*, famous in the study of heredity, has but four. It is difficult to estimate how many allelomorphs may be possessed by any organism, but they must generally number many thousands. Consequently we may expect that each chromosome will carry large numbers of them. However many may thus be associated, we should anticipate that they will all segregate together, merely because they are travelling in the same vehicle and may consequently be expected to reach the same destination.

Thus in the fruit-fly the eyes may either be of the normal red colour or of a brown shade, and the wings may be reduced from their full length to a vestigial condition. These two pairs of contrasted characters are

controlled by distinct genes which, however, are carried in the same pair of chromosomes. If we back-cross female flies (see p. 66) exhibiting the two recessives, which are brown eyes and vestigial wings, to the double heterozygotes, with red eyes and normal wings (since these are dominants), only two, instead of the expected four, classes will be formed in the R_2 generation. The reason for this is evident. Half the gametes of the heterozygotes will receive a gene $\widehat{BW}$, responsible for red eyes, together with a gene $\widehat{VG}$, for normal wings, carried in the same chromosome, while the other half will receive their allelomorphs, $\widehat{bw}$ for brown eyes and $\widehat{vg}$ for vestigial wings. The gametes of the recessive will of course all be of one kind, carrying $\widehat{bw}$ and $\widehat{vg}$. At fertilization, only the $\widehat{BW}\widehat{bw}\widehat{VG}\widehat{vg}$ and $\widehat{bw}\widehat{bw}\widehat{vg}\widehat{vg}$ combinations can be formed: that is to say, flies with red eyes and normal wings and those with brown eyes and vestigial wings, in equal numbers. The 'recombination classes', brown eyes and normal wings, red eyes and vestigial wings, are absent. But if they happen to be the classes which were crossed in the first instance, they will be the

ones which remain together. That is to say, there is no association between either type of character other than that due to the mode of transmission of their genes. The tendency for characters to remain associated, instead of segregating independently, because the genes controlling them are situated in the same pair of chromosomes, is called *linkage*.

Evidently linkage will exist between all the genes in a chromosome, however many there may be. These will all tend to be transmitted together, forming a 'linkage group'. If the chromosome theory of inheritance is true, then in any organism, the number of such linkage groups obtained purely from the results of breeding, must equal the number of pairs of chromosomes found in its cells when examined under the microscope. This condition has been fulfilled in those instances in which it has been possible to test it. Unfortunately, however, in very few species is the number of genes so far known large enough to admit of such a comparison. But in those which have been sufficiently analysed yet another striking fact emerges: it is found that the sizes of the linkage groups and the relative lengths of the chromosomes roughly correspond with one another.

The peculiar conditions which exist during the formation of the gametes will, however, suggest that linkage is rarely complete. It will be recalled that an exchange of material takes place between homologous chromosomes, or rather between the products of their longitudinal division. As we should anticipate, this exchange effects a transference of genes between them, and this is known as *crossing-over*. It is normally encountered in the study of linkage, and we may briefly consider an example of it.

In the sweet-pea, purple flower colour is dominant to red, and erect flower shape is dominant to hooded. If we cross a purple and erect flowered sweet-pea, heterozygous for both pairs of genes concerned, with a double recessive plant (having red flowers of a hooded shape), we obtain four types in the R_2 generation so produced. About 99 per cent. of the offspring are composed of the two parental classes in equal numbers, and about 1 per cent. are made up of the two recombinations between them, also in equal numbers. Since the four types are not in equality, those representing an interchange being very rare, it is clear that the genes controlling these characters are carried in the same pair of chromosomes. The exis-

tence, however, of a few red erect flowers and, in equal numbers, of purple hooded ones, shows that an occasional transference of material has taken place between the products of the homologous chromosomes, allowing about one per cent. of crossing-over. We express this fact by saying that there is a ' cross-over value ' of one between the genes in question.

If we study a number of linked factors, we find that blocks of them cross over together. Now we hold that this is due to the observed fact that the chromosomes do not twist round one another very tightly during gamete formation, so that the points of interchange are generally fairly far apart. This explanation rests upon two fundamental assumptions. First, that the genes occupy definite positions (*loci*) on the chromosomes and, secondly, that they are arranged along them in linear order like a string of beads.

We can prove both these propositions in a number of ways, though it will here be possible only to indicate very briefly the nature of a few of them : further information may be obtained from Sinnott and Dunn (13). In a constant environment, the cross-over value between any two genes is always the same. Furthermore, if a small piece (for

mechanism by which the genes are transmitted.

Finally, we may say a few words about the man on whose work the fundamental laws of heredity are based. Father Gregor Mendel (1822–84) was a member of the Augustinian monastery of St. Thomas at Brno (Brünn) in Moravia, and he lived to become its Prälat. He was a man of wide reputation in his own day but, to his great disappointment, his work on heredity was, for various reasons, ignored. He died sixteen years before the paper in which he had published it in 1866 fell into the hands of men more competent than his contemporaries to realize its value, and in a few months he had become world famous.

The greatness of Mendel's contribution lay not in his observations, but in his deductions. The very fact that others, both before and after him, had detected the segregation of characters only enhances his achievement; for they entirely failed to realize its significance. It required a man possessed of exceptional intellectual powers to draw from it the concepts of gametic segregation, of recombination, and of particulate, as opposed to blending, inheritance. If indeed he did so draw them: in a book

of outstanding importance (3)[1], Professor R. A. Fisher has discussed the theory of 'Mendelian' inheritance, and has pointed out that its essentials might have been reached by any thinker in the middle of the nineteenth century, as a piece of abstract and theoretical analysis—provided, of course, that he were endowed with mental ability of the highest order. The same author has since supplied information which suggests that Mendel's theoretical analysis may possibly have preceded his experiments: we would like to think it was so.

[1] See Bibliography.

CHAPTER III

THE INHERITANCE OF SEX

THE rediscovery of Mendel's two laws lead to work in a variety of directions which served to widen their application. We have seen in the last Chapter that it has been possible to deduce the way in which the genes are transmitted: an advance which necessitated the modification of the law of independent assortment itself. Among the earlier of these new lines of investigation, the analysis of sex occupied, and has continued to hold, an important place.

A moment's reflection will show that a close parallel exists between the facts of segregation and the reappearance of the two sexes in every generation. Maleness and femaleness indeed may be regarded as a pair of contrasted characters which segregate from one another in definite proportions. These vary in different species, and in different environments, but they generally approach equality. Now it has been shown that the sexes are controlled by one or more

pairs of linked genes. The members of the particular chromosome pair concerned in their distribution therefore play a deciding part in the determination of sex, and are known as *sex chromosomes* : the other chromosomes are distinguished from them under the name of *autosomes*.

The sex chromosomes of one sex are composed of an identical pair called *X-chromosomes*. They do not differ from the autosomes except that they carry, among others, the genes which decide whether development shall proceed along male or female lines. The other sex, however, possesses only *one* of these X-chromosomes, whose partner, the *Y-chromosome*, is abnormal. It contains but few genes, and these do not usually include any of those concerned in sex control.

The sex possessed of the two X-chromosomes, which for the present we will assume to be the female (see p. 58), will pass one of them into every gamete. On the other hand, the X- and Y-chromosomes of the male will segregate from each other, so that half the gametes will receive the one, and half the other, type. The chances then are equal that the X-chromosomes, necessarily carried by the gametes of the female, will meet

with another X, giving rise to a female (XX), or with a Y-chromosome, combining to form an XY pair which will induce male development.

It is important to notice that the Y-chromosome itself is not generally an active sex determinant. Sometimes it is absent, when one sex has an uneven number of chromosomes—the pairs of autosomes and an X-chromosome without a partner. Furthermore, owing to some failure in the mechanism of cell-division, there have been found from time to time females possessed of a Y-chromosome, as well as their two X-chromosomes, and males with an extra Y. The sex of such forms is in no way affected. This is in striking contrast to those instances in which an additional X-chromosome is included in the cells: the sex characters of such individuals are highly abnormal.

With these facts in mind, we may consider the transmission of the sex chromosomes as illustrated in Fig. 5. On doing so, a most significant fact will become apparent. That is to say, the members of the decisive X-chromosomes are not restricted to one particular sex, but are constantly shuffled across from one sex to the other in different generations. The sex of

the female is dependent upon the possession of two X-chromosomes, yet she receives one of them from her father, whose development as a male it had determined. So too, the male's single X-chromosome has been derived from his mother, where it was one of those instrumental in establishing her sex as female. Evidently the control of sex

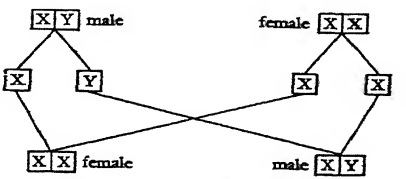

FIG. 5.—The sex of an individual is determined by the presence of one (male) or two (female) X-chromosomes, whose partner in the male (the Y-chromosome) is not normally concerned in the process. It will be seen that the control is a strictly quantitative one, since the X-chromosomes are interchanged between the sexes at successive generations.

is quantitative, not qualitative: it is maintained not by X-chromosomes of male-determining or female-determining type, but by the dosage of X-borne genes. The number carried by one X-chromosome induces male development, while twice that quantity induces female development; an observation which was one of the first to throw any light upon the way in which the genes

carried in the chromosomes control the characters for which they are responsible. We shall return subsequently (pp. 146–65) to consider this subject in more detail.

It is a curious fact that the sex carrying the XY chromosome pair is not the same in all forms. We have been discussing a situation in which it is the male, and this is the more usual condition. It obtains in the class of animals (the Mammalia) to which we ourselves belong, so that it is the father, not the mother, who is responsible for the sex of his offspring. In some groups, however, including birds, butterflies and moths, and a few others, the male possesses the two X-chromosomes and the female the XY pair. The sex determination mechanism is here reversed, so that birds lay two kinds of eggs, one producing males and the other females. Owing to this singular lack of uniformity, it is necessary to have terms distinguishing the two types of individuals, whatever their sex may be. That carrying the XY pair we call the *heterogametic sex* (producing unlike gametes), in distinction to the *homogametic sex* with the two X-chromosomes.

In addition to acting as sex determinants, the X-chromosomes, as the autosomes, carry an assortment of genes affecting a wide range

of characters. These, however, will be inherited relative to sex ; for they are included in the same linkage group with the sex genes and, consequently, are *sex-linked.* We must examine the peculiar conditions to which such genes are exposed.

When two X-chromosomes are present, a recessive sex-linked character can only be expressed when homozygous, so that it does not differ from the ordinary autosomal situation in this respect. In the heterogametic sex, however, the genes of the X-chromosome are opposed only by the relatively empty Y-chromosome. Here most of the recessives will exercise their full effect even in single dose, for their action cannot be obscured by a dominant partner. In ourselves, where the male sex is heterogametic, a father can transmit his sex-linked genes only to his daughters, for the single X-chromosome which his sons possess is derived from their mother (Fig. 5). A daughter, on the other hand, inherits her sex-linked genes equally from her two parents.

A notable example of sex-linkage is provided by the ' Hesse Disease ', which is rather widely spread in the Royal Families of Europe. It is technically known as hæmophilia, and its symptoms are due to

imperfect clotting of the blood. This leads to various forms of hæmorrhage, bleeding into some of the joints generally takes place, causing stiffness, and death occurs at an early age. However, an affected individual occasionally lives long enough to marry and, since the condition is recessive, he will have normal children. His sons will be perfectly free from the taint, for they do not receive an X-chromosome from their father; but his daughters, being heterozygotes, can transmit it to their descendents. When they marry, half their sons and half their daughters will receive the X-chromosome carrying the hæmophilia gene, and the other half will receive its normal allelomorph. Consequently half the sons will exhibit the disease and half will be normal in heredity as well as in body. All the daughters will again be normal, but half of them will be heterozygotes.

It is evident, therefore, that if a man inherits the gene for hæmophilia he is bound to suffer from the disease. If he is healthy, even though of unsound parentage, he need not fear that he may transmit it to his descendents.

Hæmophilia can very rarely affect the female sex. For it to do so, a heterozygous woman must marry a hæmophiliac. All

four types of offspring will then be produced in equal numbers : sons and daughters with hæmophilia, normal sons and normal, but heterozygous, daughters. Obviously such a marriage will very rarely occur, and it is doubtful if, in fact, it has ever taken place. Furthermore, were it to do so it is open to question if the affected daughters would survive, for it is possible that two doses of the hæmophilia gene might have a greater effect than one.

A number of other sex-linked characters have been studied in man. The majority of them involve grave diseases, though one, at any rate, is comparatively innocuous ; this is the common form of red-green colour-blindness. As in all such characters, the condition is much commoner in the hetero-gametic than in the homogametic sex, although it is not necessarily restricted to the former. Colour-blind women can of course arise in the same manner as that postulated for hæmophilia ; by a marriage between a normal, but heterozygous, female and a colour-blind male. Here too, half the daughters, as well as half the sons, would be colour-blind. Were such a colour-blind woman to marry a colour-blind man, all their offspring would be colour-blind : for

the three X-chromosomes involved (two brought in by the mother and one by the father) would carry the gene concerned.

Many instances of sex-linkage have been studied in other animals, not only in forms in which the heterogametic sex is the male but also in those in which it is the female. We may profitably consider an example of the latter type, both to demonstrate the strict reliance of this kind of inheritance upon the sex-determination mechanism and its independence of sex as such, and to illustrate a further general property of sex-linked characters.

In poultry, barred plumage in the domestic fowl is dominant to the non-barred condition, and the gene controlling it is carried in the X-chromosome. It will, however, be remembered that the female possesses the XY pair in birds. Consequently, if a heterozygous barred cock be mated to a non-barred hen, all four types will be produced in equal numbers. We have made the same kind of mating as that which gave rise to colour-blind females in the human species, except that the dominant and recessive characters are here necessarily reversed relative to sex.

This instance provides us with a good

opportunity to investigate another important cross. If we mate a barred hen with a non-barred cock, all the male offspring will inherit their mother's character and be barred, while all the females will inherit their father's character and be non-barred ('criss-cross inheritance'). If the non-barred bird which we select has black feathering, the two types are easily separable in the down plumage. Such a mating therefore allows us to recognize cocks and hens among the chicks before their other sexual differences become apparent. The sex-linked characters gold (recessive) and silver plumage can be used in the same way: the two classes of chicks being readily distinguishable.

The inheritance of sex allows us to obtain some insight into the way in which the genes may operate. We have already been able to deduce that the deciding element in its control is the total number, not the kind, of genes carried by the X-chromosomes. We will now discuss a series of investigations which enable us to carry this analysis rather further.

The fruit-fly *Drosophila melanogaster* belongs to an order of insects (the Diptera) in

which the sex-determination mechanism is of the more usual kind, the female having the two X-chromosomes. In certain instances, flies have been found which, owing to some accident of cell-division, possess an extra X-chromosome, three instead of two. The female characteristics of these individuals are developed in an exaggerated degree. Furthermore, it is possible to destroy pieces of chromosomes by means of X-rays (see Chapter 4), so that flies can be studied in which, though the normal number is present, one of the two X-chromosomes is incomplete. These are to some extent intermediate in sex, showing distinct traces of male characters. The larger the piece that is missing, the more pronounced is the approach towards maleness. Finally, when one X-chromosome is altogether absent, we reach the condition of the heterogametic sex and a normal male results. These facts evidently demonstrate that the genes in the X-chromosomes are female determining. Consequently, as the proportion of them increases, so the individuals concerned pass progressively from the condition of a normal male to that of a normal female, which they finally exceed.

Similar accidents of cell-division have

provided specimens with three, instead of two, sets of *all* the homologous chromosomes. These prove to be quite normal females: the extra X-chromosome no longer gives rise to sexual abnormalities when an extra compliment of autosomes is present also. We are immediately confronted by the suggestion that the autosomes are male-determining, and that a balance exists between them and the female-determining X-chromosomes; one which is confirmed by a study of further irregularities of the same kind.

For example, instances have been found in which specimens have acquired three sets of autosomes but only two X-chromosomes. The latter condition is that of the normal female, but such specimens are intermediate in sex: there are too many of the male-determining autosomes. When one X-chromosome exists in the presence of three sets of autosomes, the male characters become developed in an exaggerated degree. On the other hand, the loss of portions of any of the autosomes produces a tendency towards the development of female characters in males.

These results make it clear that sex is determined by a balance between a normally fixed dosage of male-determining genes,

carried in the autosomes, and a dosage of female-determining genes carried in the X-chromosomes. This is varied in amount by the mechanism which distributes either one or two of them to each individual.

When pieces of any of the chromosomes are destroyed, the degree of sexual abnormality which arises is roughly proportional to the extent of the loss. This fact indicates that the sex-genes must be both numerous, approximately equal in effect, and fairly evenly distributed. For this reason, it is essential that those in the X-chromosome should not become scattered by a transference of the material containing them across to Y. Consequently, crossing-over between these two chromosomes is restricted to a small section only. The mechanism which ensures this may incidentally reduce, to a varying degree, the amount of crossing-over between the autosomes in the heterogametic sex. It does so to an extreme degree in *Drosophila* in which practically no crossing-over occurs in the male (p. 46).

We have described several situations which lead to the production of individuals intermediate in sex. When such specimens are studied critically, it is found that they are not in reality intermediate in all their parts,

but are made up of a mixture of male and female regions. One or the other of these greatly predominates if the departure from normality is but slight. A further examination shows that when one sex begins to assume the characters of the other, those inappropriate to it are the ones which develop latest. As the degree of intermediacy increases, structures formed earlier are progressively affected until the greater part, and finally the whole, of development may fall within the control of the opposite sex. The latter condition of course leads to a sex reversal.

Now either sex is capable of taking on the characters of the other, since either can become intermediate.[1] It is clear, therefore, that the sex genes decide which type of development shall be initiated and pursued by individuals potentially capable of assuming either male or female characters. Furthermore, the fact that sex intermediates are possible, and in varying degrees, demonstrates that a mere excess or deficit of the products of one type of gene over the other is not enough to establish normal sex. Evidently the two types of sex genes produce sub-

[1] Such a conversion is nearly limited to the female in *Drosophila*, but for special reasons only.

stances which must be in excess of one another by a given amount before complete sexuality can be attained. If they fail to do so, we see that the concentration of the wrong sex-determinant will catch up and surpass that of the correct one during development. All structures formed before this *turning-point* will be of one sex, all those formed after it will be of the other. The more that the sex-determining substance falls short of the necessary amount, the earlier will this turning-point occur, and the larger will be the number of structures whose development takes place subsequently to it. Such individuals as these, which have developed for a certain time as one sex and then switched over to continue their development as the other, are called *intersexes*.

It is apparent then that the sex-determining genes control the time of onset and the duration of alternative processes in the body. Like any others, they are capable of existing in different allelomorphic states and, since their action is quantitative, this will either diminish or intensify their efficiency in establishing the characters of the sex for which they are responsible. We have already mentioned that in *D. melanogaster* they are very numerous and fairly uniform in their

action, so that the results of their individual segregation will not be detectable. We know, however, that such segregation takes place for different strains can be built up in which the effect of a particular degree of intersexuality (say that resulting from 2 X-chromosomes to 3 sets of autosomes) is respectively very marked or very slight. Since the normal development of males and females is based upon a *balance* between the genes concerned, the sex control would not be hampered if both male- and female-determining genes were proportionately weakened or strengthened by recombinations. However, no such situation could become established in such an animal as *Drosophila*, which is not split up into groups. For the balance would be upset if matings were to take place between specimens with different absolute (but similar relative) values of the sex determinants, as they would be bound to do in a mixed population.

On the other hand, when a species forms local races, there is no reason why these should not acquire different values of the male and female controlling substances, owing to the substitution of different allelomorphs in the genes producing them, so long as their relative relationship to one

another is preserved. This state of affairs is actually realized in the Gipsy Moth (*Lymantria dispar*). In this species a number of races are known to exist in Europe, continental Asia, and Japan, which, when crossed, produce intersexual individuals segregating in definite proportions. Now it is important to notice that no such abnormalities occur within the races themselves: only when individuals belonging to one are crossed with those belonging to another. The sex-determination mechanism is perfectly adjusted within each, but not throughout the species as a whole. Here then we have an instance of different absolute values being assumed by the sex determinants in different regions. What this involves may be explained in the following way. If the genes in the X-chromosomes produce 20 units of one sex-determining substance, which are balanced against 30 units of the other, there will be a definite excess of one or the other type, whether one X-chromosome is present or two. The same condition will be fulfilled in another race if the values are respectively 30 and 45 units. But confusion would result if the two were crossed; for the fixed dosage of 30 units possessed by one race could then be balanced against the X-chromosome of

the other, also carrying 30 units; neither type would be in excess, and intersexuality would ensue. It is, in fact, possible to arrange matings between individuals with different high and low values of the sex determinants so as to produce any required degree of intersexuality either in the males or females.

The differences between the sex-determination of *Lymantria* and *Drosophila* are superficial, and only two of them need be mentioned. *Lymantria*, being a moth, belongs to the group having an XY pair in the female. Consequently the X-chromosome must carry male-determinants balanced against a fixed amount of the female determinant—the reverse condition to that of *Drosophila*. Secondly, the female determinant is not carried in the autosomes or, rather, the predominant quantity of it is not. (The existence in them, however, of genes influencing the degree of male intersexuality may represent a relic of an original *Drosophila*-like control.) Crosses between different races show that the major part of the female determinant of *Lymantria* is maternally inherited. It may therefore be carried either by the cytoplasm or by the Y-chromosome, both of which are restricted to this

sex. Goldschmidt, to whose brilliant work the whole analysis of sex in *Lymantria* is due, now supports the former of these alternatives, but this view is not universally accepted.

It has already been pointed out that the end-product of intersexuality is a reversal of sex. This is attained when the turning-point occurs so early that the whole course of development is subsequent to it. Now by crossing two Japanese races of *L. dispar*, which chance to have respectively the lowest and highest absolute values of the sex-determinants known, the turning-point may be advanced to this degree. Males converted into females are easily obtained, and females turned into males are sometimes produced ; though the latter type is rare because very delicate. Such specimens have of course their original chromosome constitution : XY in those transformed into males and XX in those which have become females. Evidently the distinction between the two types of sex control, with the XY pair in the male or female, respectively, is more apparent than real. As we see, it is even possible to convert the one into the other experimentally, for the situation merely depends upon the balance of sex genes involved.

Irregularities of division in the germ-cells may provide an individual with an abnormal outfit of chromosomes, and we know that this sometimes leads to intersexuality. When such defects occur in the body cells, sexual abnormalities of another kind may be produced. In the homogametic sex, a cell may lose one of its two X-chromosomes owing to a defective division at some stage in development. Its products will then be equipped with a single X-chromosome only. This is the condition of the heterogametic sex. Consequently, male and female cells will coexist, and organs of different sex will develop side by side in the same individual. Should the accident which leads to this state of affairs occur at the first cell division, the male and female parts will be in equal amounts. Where the first two cells of the embryo give rise to the right and left halves of the adults, as in insects, the two sides will be of opposite sexes; and they are often quite sharply separated from one another down the middle line. If the chromosome irregularity occurs late, it will affect only a small region of the body. Individuals of this kind, in which parts of different sex develop simultaneously, are called *gynandromorphs*. It will be recalled that in intersexuality, male

and female development never proceeds concurrently; the whole individual being first of one sex and subsequently switching over to the other. As Goldschmidt has succinctly expressed it, an intersex and a gynandromorph are sex abnormalities in time and in space, respectively.

The existence of gynandromorphism in many forms, for example the insects, makes it clear that in them the sex of every cell of the body is determined independently by its own chromosome outfit. The type of sex-gland present, whether it be a testis producing spermatozoa or an ovary producing eggs, can, in these circumstances, have no bearing upon the general sex-characters of the individual. This fact has been established also by direct experiment. Even in insects, it has been possible to remove the sex glands of one sex and to replace them with those of the other. It is found that the remaining sex characters are in no way influenced: not even in a male whose body is full of eggs.

This situation, however, is not universal. In all vertebrate animals the sex glands pass into the blood substances which circulate throughout the body and modify the rest of the sex characters. Evidently the kind of operation which we have just mentioned will

have a much more profound effect here. Simple removal of the sex glands will prevent further sexual development, while a subsequent grafting of those of the opposite sex will reverse the sex of all those characters not yet irrevocably established.

In forms such as these, the XX-, XY-chromosome mechanism determines not the sex of every cell but whether male or female sex glands shall develop from an undifferentiated rudiment. The sex of the remainder of the body is then partly or wholly handed over to their control, so being influenced by the sex-chromosomes only indirectly.

The degree to which this process has been carried varies in different forms. In the mammals the action of the sex-chromosomes seems almost completely limited to initiating the development of the sex glands along male or female lines. Here gynandromorphism is hardly possible, for the sex of a cell does not depend upon its own chromosomes. However, in birds and other vertebrates, the part played by the sex-chromosomes is somewhat less restricted.

The existence of the XX-, XY-chromosome mechanism seems perfectly adapted to secure the numerical equality of the sexes.

That this is in reality rarely attained, is a fact which demands attention. In the human species, the secondary sex ratio, which is that found at birth, shows a slight but quite definite excess of males : in England at the present time it is approximately 105·6 : 100. Now this disparity is known to be much greater at conception (the primary sex ratio). It is, however, reduced by a differential elimination of the male sex, which continues after birth and results in equality in late adolescence. The same tendency maintained throughout life leads to a subsequent, and gradually increasing, excess of females, so that there are actually more than twice as many women as men among those aged eighty-five and over.

We have here proof of a constitutional difference in vigour between the sexes. Its effect varies in degree in different races and environments. Unfavourable conditions both before and after birth tend to accentuate, and favourable ones to obscure, it : thus the proportion of girl babies is higher among the children of older than of younger mothers.

In order to explain these facts, we have to solve two problems : why the sex ratio is not equal at conception, in spite of the mechanism which seems so well fitted to

ensure that it should be so, and why the male sex is more delicate than the female. The latter is the more open to analysis, and we may consider it first.

Now recessive characters are generally disadvantageous (see Chapter VIII), and most of those controlled by genes carried in the X-chromosomes will be free to exercise their effect in the heterogametic sex; in the homogametic sex, however, they will be unable to do so unless present in double dose. It seems, then, that the very mechanism of sex determination necessitates a weakness of the sex with the single X-chromosome which, it will be remembered, is the male in man and other mammals. But this tendency seems to be insufficient to account for the facts; for as far as we know, in birds, and in butterflies and moths, the females remain in excess, though here they are the heterogametic sex. It can be shown, however, that males, whatever may be their chromosome constitution, consume more energy than females (their ' metabolic rate ' is higher), and their lower resistance may well in part be due to this greater expenditure.

The inequality of the sexes at conception is a more difficult matter to study, but an

illuminating suggestion, put forward lately by Professor F. A. E. Crew, serves to explain it with reasonable probability. It is known that genes exist which act differentially upon the X- and Y-bearing spermatozoa, tending to produce an excess of one or the other. Selection may have spread those benefiting the Y-bearing type sufficiently to counterbalance the deficiency of males. This would be adjusted to the degree best suited to each species. In man, it might be expected to involve a numerical equality in the sexes at the time when, in a primitive society, reproduction takes place: and it is at this age, and then only, that such equality in fact exists. It necessitates, however, that the Y-bearing spermatozoa should be so favoured as to produce that excess of males at conception which we encounter in the human race.

CHAPTER IV

MUTATION

WE have seen that each gene can exist in a number of different states, so that the pairs of allelomorphs may be made up of similar or dissimilar members. The change which occurs when it passes from one of its phases to another is called a *mutation.* However, this term is not restricted to alterations in the genes, but is extended to cover those taking place in any hereditary unit. For example, the chromosomes are transmitted from generation to generation, and they carry the genes. Should a part of one of them break away, the characters of those individuals which inherit the remaining portion will be affected, and the breakage constitutes a mutation. We may therefore define a mutation as *a change in any unit of heredity.* It is important that this definition should be strictly applied. As we shall see (Chapter V), inherited characters are occasionally controlled cytoplasmically. The term must be applicable also to the units carried in this

way: it must not be limited to the genes and chromosomes. So too, it must include changes in the units employed in any hypothetical method of transmission, so that this can be justly compared with the system proved in reality to exist. We shall see the value of this procedure in Chapter X, when we discuss the evolutionary significance of the hereditary mechanism postulated by Darwin. As far as its effect on the whole organism is concerned, it must evidently be limited to changes in the hereditary units themselves. Mere changes in the hereditary constitution can, of course, occur by other means: that is, by recombination.

Nor must other extremely important properties of mutation be brought into its *definition*. Two of these may appear to be fundamental, that the process is sudden and that it is very rare; but they are only superficially so. The suddenness of mutation is an observed fact, but we must reserve to ourselves the right to say that a gene (for instance) mutates gradually, should it ever be found to do so: so far it has not. In point of fact, we do not certainly know whether the exceptional cytoplasmic mutations are, or are not, sudden. As we shall see (Chapters V and X) the rarity of mutation

is dictated by the type of hereditary transmission found to prevail in living organisms. We shall be greatly handicapped if we cannot analyse the effect which frequent mutations would have, and compare it with that obtained when they are rare.

The space taken in defining mutation is very necessary, for the term is often used quite loosely, leading to confusion. It has been employed in three distinct senses. First, in older literature, an *individual* was called a mutation if it exhibited any exceptional character, more or less presumed to be inherited. There is no need on this account to abandon the name to-day. Biological nomenclature is full of words formerly employed loosely, but now more strictly defined. There is no need to discard them because they were adopted before the situations which they label had been analysed, and their significance had to be restricted to certain aspects of them. Secondly, mutation is correctly employed in the manner just indicated. Thirdly, it is surprising to find it constantly used even by careful writers on genetics [1]

[1] Genetics is the study of heredity and variation. The term has not been employed elsewhere in this book, as it is desired to reduce the number of technical words as far as possible. It has been used pur-

to mean the changed gene which has resulted from a mutation (in the strict sense), or even the character to which it gives rise. Thus the normal eye-colour of *Drosophila melanogaster* is red ; a specimen with white eyes is often called a mutation. On the contrary, the act of change, by which the gene normally producing red eyes passes to another phase (giving rise to white eyes), is the mutation—nothing else is. It is none the less convenient to possess terms indicating the gene to which a mutation gives rise and the character which this produces. ' Mutant gene ' and ' mutant character,' already loosely used in this sense, may be strictly applied for this purpose.

In Chapter VII we shall see that the distinction between gene mutations and chromosome mutations may hardly be a real one. It is, however, convenient to treat them separately in the present account.

It has already been mentioned that the genes undergo mutation very rarely, though of course the process is ultimately responsible for the existence of different allelomorphs at the various loci. Its actual frequency in normal conditions is a difficult thing to

posely on this occasion, so that students who meet it in subsequent reading will understand its significance.

estimate. On the whole, however, it seems that mutation may occur at a particular locus in somewhere between one chromosome out of a million and one out of ten million in every generation. Normally, therefore, we can hardly expect a given gene to mutate more often than in one individual out of half a million. Little as we know of this subject, it is clear that all the loci do not undergo mutation at the same rate. If we except one or two instances, of apparently 'unstable genes', the highest mutation rate for any known locus in *D. melanogaster* is about 1 in 300,000. This occurs in the series of multiple allelomorphs which produce eye-colours leading down from the normal red shade to white.

It appears, then, that the different genes vary in the rate of their mutation, but that the process is a recurrent one. Consequently, a particular 'mutant gene' is produced with a definite frequency, so that the species has in the long run repeated opportunities of incorporating and using it, should such a course be desirable (Chapter VIII).

The number of organisms in which we can form any direct estimate of the mutation rate is quite small. However, these few

represent exceedingly diverse types, and include both plants and animals. Though there is some suggestion that the actual level of mutation may differ among them to a minor degree, it remains throughout fundamentally the same. We may feel confident, therefore, that the process is always a very rare one. This indeed is to be expected on general grounds, if in fact the main body of organic inheritance is of the kind already described : a point which will be explained in the next chapter.

As will become clear when we consider the evidence obtained from the artificial induction of mutation, the nature of the change occurring at any locus appears to be unrelated to external agencies. Thus a gene which has already arisen by mutation may, by the same process, revert to that from which it was derived. There is nothing to suggest therefore that the genes possessed by the normal individual differ fundamentally from those whose origin by mutation we have encountered in experimental work. The change can take place from the ' normal ' to the ' abnormal ', or the reverse. Indeed, when we have discussed the effects of selection and the course of evolution in Chapters VIII and X, respectively, it will

become plain that no such fundamental distinction is to be expected. It may be desirable, however, to give a concrete example of reverse mutation in an animal and in a plant. Such instances could be cited in numbers.

Dilute pigmentation in the house-mouse is a recessive condition due to a gene which has changed by mutation. Keeler has studied its reversion back to the normal allelomorph, producing the dominant intense colour. This took place in the germ-cells of an individual of a 'dilute' strain, so that among its offspring there appeared one of normal coloration. This specimen was proved to be heterozygous for the allelomorphs concerned. Furthermore, the family was homozygous for a second recessive character (short ears). This was present in the mutant specimen. It is clear, therefore, that the result cannot be explained by the accidental introduction of a normal mouse.

In wheat, a single pair of allelomorphs causes delay in the development of the green pigment (chlorophyll), the condition being recessive. Neatby has demonstrated the mutation of this gene back to that producing normal dominant chlorophyll development, in circumstances which preclude the pos-

sibility of accidental crossing: a normal seedling appearing among a crop of abnormal ones. In other instances he found that the reversion took place not in the germ-cells but in a body-cell, giving rise to an abnormal section in an otherwise normal plant. Here experimental error can be excluded. This is an example of an important fact: that mutation may occur in the body-cells 'somatic' mutation as well as in the germ-cells. This has often been studied in animals, especially in *Drosophila*. In plants it is especially important, for in them the portion involved may be propagated by cuttings. In animals there is a clear distinction between the body-cells and germ-cells. The former are set apart at an early stage in development, and subsequently remain distinct. In plants this is not so. Flowers can therefore be obtained from such cuttings, and the type of change involved in a mutation of the body-cells can thus be investigated by experimental breeding.

Mutation supplies the basis of inherited variation, so that its importance is very evident. Many investigators have therefore attempted to modify the process artificially. Furthermore, any very rare phenomenon is

difficult to study, and the possibility of increasing its frequency sufficiently to subject it to various quantitative investigations was a very attractive one. None, however, succeeded until H. J. Muller showed in 1927 that mutation in *D. melanogaster* can be increased about 150 times by X-rays. His brilliant achievement has made available a certain and effective means of inducing mutation, in a manner which gives consistent and measurable results. For this purpose he has elaborated a highly specialized technique, and we must now briefly consider the more important deductions which can be drawn from this work.

It is now known that all types of short-wave radiations give rise to mutations: X-rays of varying wave-lengths, ultra-violet rays, the γ-rays of radio-active substances, also free electrons (β-rays of radium). These agents are all equally effective, provided that equivalent doses (judged by ionization rate) are employed. It is of course especially difficult to use ultra-violet rays, owing to their low penetrating power. It is found, furthermore, that the relationship which exists between the amount of radiation and the rate of mutation produced is of the simplest kind, being in direct proportion.

A doubling in the X-ray dosage results in the production of twice as many mutations.

All types of mutation can be induced artificially, and they can occur anywhere in the body. Chromosome and gene mutations are both produced, and they may take place in the germ-cells, gametes, or body-cells alike. Furthermore, changes similar to those which have been encountered spontaneously arise when short-wave radiation is applied. Naturally, as their frequency is so much higher, some are encountered which have not yet been detected in normal circumstances.

No difference in the type of mutation produced results from varying the dosage, or the kind of radiation, employed. Since the effect is purely a direct one, in the sense that no residual tendency to mutation remains when the treatment has been suspended, we may conclude that a simple relation exists between the hit of an electron and the induction of a mutation: a fact which is strongly supported by the simple proportionality between dosage and result already indicated. Indeed, the influence is an entirely local one. When one gene mutates, there is no tendency for those on either side of it, nor even its allelomorph, to do so.

However, not all loci are affected with the same frequency. Those which mutate most often under treatment are the ones in which spontaneous mutation most frequently occurs.

Though by far the most intensive work has been conducted on *Drosophila*, it has been established that organisms of the most diverse kind respond to short-wave radiation in a similar way. A large number of animals and plants have now been subjected to analysis, including such widely distinct forms as fungi, maize, *Antirrhinum*, *Habrobracon* (a parasitic wasp), and mice.

A most important fact must be noticed here. That is to say, reverse mutation back to the normal condition can be produced by X-rays, both from genes which mutated under its influence and those which did so in ordinary circumstances. One or two authors have maintained that gene and chromosome mutations are abnormal processes, involving only damage to the chromosomes, and they hailed their production by such a ' destructive agent ' as X-rays as a proof of this view. Such a contention cannot be sustained in face of the facts of reverse mutation. If X-rays damage the chromosomes, they are able also to repair them !

It is clear, therefore, that short-wave

radiation increases the rate of a process occurring naturally, and that the mutations which it produces are of no abnormal kind. It was consequently suggested that the existence of mutation in nature is due to the small amount of short-wave radiation ordinarily available. It has, however, been calculated that low as is the spontaneous mutation rate, it is far too high to be accounted for in this way. The cause of natural mutation therefore remains unexplained.

We must now give some attention to chromosome mutations. These can be divided into three main types. First, those in which a chromosome breaks; secondly, those which lead to the presence of an extra chromosome, or to the loss of one from the nucleus ('heteroploids'); thirdly, those multiplying the total number of chromosomes. All of them may occur spontaneously, or they may be induced by short-wave radiation. They must each be briefly considered.

It sometimes happens that a fragment of a chromosome may break away and become reattached elsewhere, either to the homologous chromosome or to one of the other pairs. The former condition gives rise to *duplication*, and some of the loci are of course

repeated in the chromosome so formed. This gives an opportunity for increased variation, since different allelomorphs of the same gene may be carried together. However, such abnormalities can rarely be established as a pure-breeding strain, for individuals in which they exist in the homozygous state are generally very unhealthy. This applies also to the reattachment of fragments to a non-homologous chromosome ('translocation'). Such a condition provides a striking proof of the physical basis of heredity, for the interchange can be inferred by the linkage of genes to others of a group to which they do not belong. On the other hand, the addition of material to one of the chromosomes gives rise to an inequality which can sometimes be detected under the microscope, as can the longer duplications.

Translocations may sometimes be reciprocal. That is to say, the ends of non-homologous chromosomes may exchange material. The pairing of homologous units during gamete formation will then hold together those which were originally separate chromosome-pairs, or sets of chromosomes —if the process has taken place repeatedly. In this way genes in distinct chromosomes may become linked with one another.

Occasionally a fragment rejoins the wrong way round with the chromosome from which it was derived. In such regions, homologous genes do not lie opposite each other, and crossing-over between them cannot take place.

In the instances so far mentioned, the fragment of chromosome which has broken away has succeeded in reattaching itself elsewhere. Sometimes, however, it fails to do so and is lost. This leads to ' deletion ', in which some of the genes, for example in an autosome, find themselves unopposed by their allelomorphs, in the same way as sex-linked genes in the heterogametic sex. All those having recessive effects are detectable in such segments, since their action cannot be obscured by a dominant partner. Finally, we may mention those instances in which two chromosomes become attached to one another without any other anomaly, so far as can be judged. Thus a race of *Drosophila melanogaster* has been established in which both X-chromosomes are fused together. Consequently females receive their two X-chromosomes from their mother, and males inherit their single X from their father, so resulting in a reversal of sex-linkage.

It has recently been shown that the occurrence of chromosome fragmentation is

often associated with gene mutation at the point of breakage. Furthermore, we know that the effect which a gene produces in a new situation is not always quite the same as that to which it normally gives rise. Evidently the genes are not wholly isolated from one another in their operation, a point to which we shall return when we discuss their nature and action in Chapter VII.

Heteroploids are those forms in which a single chromosome has been added or lost. They generally produce marked and very disadvantageous effects, since they upset the balance of the genes which, as we have seen in discussing sex determination, is carefully adjusted. For example, a number of distinct forms of the thorn-apple (*Datura*) are known ; in each of them one of the chromosomes is represented three times instead of twice. In heteroploids, the pollen grains carrying the extra chromosome are generally less hardy than normal and often are unable to survive. So, too, the loss of a whole chromosome is evidently an extremely dangerous occurrence and usually leads to death. However, *Drosophila melanogaster* possesses one very minute chromosome pair, and individuals can survive with one, but not both, of its members absent.

In normal circumstances, the body cells of an organism possess two chromosomes of every kind, and gametes one only. These are called 'diploid' and 'haploid' types, respectively. 'Polyploids' are those which possess more than two complete sets of chromosomes.

Now large numbers of plants, and even a few animals, are undoubtedly polyploids. When the condition arises in cultivation, the affected plants prove to be larger than normal, but less fertile. Indeed, the size of their flowers makes them valuable subjects for the horticulturist. However, not only is their fertility poor, but they are nearly always sterile with the diploid form from which they arose. It is now known that they can be produced vegetatively as shoots from wounded callus. Thus by repeatedly cutting back decapitated tomato plants, Jørgensen was able to raise the proportion of polyploids appearing among the resulting shoots to as much as 10 per cent. These were of the type containing four sets of chromosomes ('tetraploids').

It is also possible to produce haploid forms; but not by this means, for their appearance is associated with sexual reproduction rather than vegetative growth. If

two species are crossed, male gametes incapable of affecting fertilization may sometimes stimulate the egg to develop ' on its own ', so giving rise to a haploid plant or animal.

The polyploids so far discussed show but few striking characters save greater size, for their chromosome balance is not upset. They belong to the group called *autopolyploids*, in which all the sets of chromosomes are derived from the same species. More striking, however, are the *allopolyploids*, which result from chromosome doubling after hybridization.

When two species are crossed, the offspring possess the haploid chromosome set of each. They are sterile, since the chromosomes find no homologous members with which to pair. Should they double their number, however, the ' allotetraploid ' plant so formed becomes fertile, as each chromosome now possesses a partner. In this way may arise very distinct forms, sterile with their parents but fertile with their own type. Indeed, they constitute a new species, whose sudden origin by this means has several times been witnessed, and it has unquestionably taken place in nature (pp. 225–6) Thus *Primula Kewensis* is a perfectly distinct

species from its parental forms *P. floribunda* and *P. verticillata*, from which it arose in cultivation, and it cannot be crossed with them.

Finally, we must say a few words about plant chimæras. Either by grafting or by somatic mutation, individual plants may be built up of two or more hereditarily distinct parts. Often the skin is of one kind and the core of another. Here and there the position of the two types may be reversed, giving rise to patches of different constitution. Such plants are called " chimæras '. Their seedlings do not reproduce the chimæral pattern nor do cuttings from the roots, which always give that to which the core belongs. They may, however, be perpetuated by cuttings of other parts.

In general, it will be appreciated that the effects of chromosome mutations are disadvantageous, though polyploid forms may sometimes successfully establish themselves. Indeed, they are widespread in plants, but rare and unimportant in animals. This is due to the fact that the mutation is rare, while the individual produced is generally fertile only with its own type. Often this is no great drawback in plants, but in animals it makes the spread of polyploid forms almost

impossible. It has, in addition, been pointed out by H. J. Muller that the balanced sex-determination of animals is a great handicap to the formation of polyploids in this group. A few species which must be polyploids are certainly known in animals, but it is still doubtful how they have been produced.

CHAPTER V

THE NATURE OF HEREDITY

WE have so far limited our discussion to the particulate or 'Mendelian' type of inheritance, and to the consequences of the fact that the genes are carried by the chromosomes. Now it is theoretically possible to imagine a number of other ways in which heredity might be controlled. Therefore, before we begin to apply at all widely the system which we have so far studied, we must carefully consider whether we have to take any of these into account, or whether we are justified in regarding the particulate mechanism as playing at least a major part in organic inheritance as a whole. Fortunately this task is simplified by the fact that all possible hereditary mechanisms fall within a few natural groups. We must enumerate these and briefly consider the claims of each.

At the outset, it is evident that heredity may either be bisexual or under the control of one of the two parents only. Experimental studies have indicated that the former

basis is correct, but the number of characters whose inheritance we can directly investigate must, after all, form but a small proportion of the whole, even in the most suitable species. Evidently we need some general test for the existence of unisexual inheritance before we can rank it as rare enough to be of negligible importance, and, fortunately, such a test is not difficult to find.

It is possible to calculate mathematically a quantity known as the *correlation coefficient*, which tells us whether or not the variation of two characters is independent, and provides a measure of the extent of any association, or *correlation*, which may exist between them. Furthermore, we can obtain an estimate of the error to which this calculation is exposed, as well as that involved in comparing two such correlation coefficients. Now instead of studying the relation between two different characters, say hair-colour and height, in one group of individuals, it is equally possible to measure the degree to which the variation of one character is associated in two groups of individuals. This enables us to compare correlation coefficients obtained between near and between distant relations. When we do so, we find that the variation of any character in two groups is

more independent when they are distantly than when they are closely related. The correlation coefficient therefore both establishes the existence of heredity, even in instances outside the field of possible experiment, and provides a comparative measure of its intensity.

We can now carry our analysis an important step forwards. Suppose we find to what degree a character is correlated first between a group of individuals and their male parents and, secondly, between the same group and their female parents. If any considerable part of the heredity involved is unisexual, then the two coefficients will differ significantly. That they do not do so indicates that the bulk of inheritance is bisexually controlled, whether we can study it experimentally or not.

This fact throws light upon a problem which will already have occurred to the reader. We have seen that hereditary factors are carried by the nucleus: are we to think that they are transmitted also by the cytoplasm? The answer to this question has just been provided. It will be recalled that the share of nuclear material carried by the male and female gametes is equal, but that the amount of cytoplasm

which they possess is extremely different, being relatively minute in the male type. If, therefore, any considerable part of organic inheritance is determined by factors carried in the cytoplasm, the female would contribute far more to the heredity of her offspring than the male, which, in fact, she does not do.

Now although we can assert that the cytoplasm takes a quite subordinate share in hereditary transmission, we are not to suppose that it plays no part at all in this process. We may therefore briefly consider a few instances of cytoplasmic inheritance.

The twist of a snail shell may turn either to the right or to the left. The latter is rare, but though many species are wholly 'dextral', a few are wholly 'sinistral', while in some both types are found. The latter condition has been studied in detail by Captain Diver and others. Ignoring certain complexities, their analysis showed that dextrality and sinistrality are controlled by a single allelomorphic pair, dextrality being dominant. However, the circumstance which demands our attention is this: the gene determining the twist elaborates into the cytoplasm of the egg a substance which decides its direction in the *offspring*. I sus-

pect that in special circumstances (pp. 110–11) a similar phenomenon may be rather widespread, but it hardly constitutes cytoplasmic inheritance as such. The effects on the cytoplasm of the genes of one generation are not carried beyond the next and, in reality, we encounter here only a delayed nuclear inheritance. This condition is really analogous to the transference of substances from mother to embryo in a mammal by way of the ' placenta ' which connects them. By repeated and increasing doses, it is possible to raise very greatly the resistance of the body to certain drugs. Such resistance is sometimes transmitted in a progressively attenuated state for one or two generations in the female, but not in the male line. This is hardly inheritance at all : the offspring have merely been dosed with a substance during development.

However, in a few instances, cytoplasmic inheritance of a more definite kind is recorded ; of this, plants provide by far the most important example. Their green colouring matter, known as chlorophyll, is contained in self-perpetuating bodies, the chloroplasts, carried in the cytoplasm. If these should be imperfectly developed or absent, the offspring cannot create them

anew: it depends for its original supply upon those which it receives in the cytoplasm of the ovule. Thus Correns studied a race of the Common Four-o'clock (*Mirabilis jalapa*) in which the leaves were variegated with white. Self-fertilized flowers on a green branch produced only true-breeding green plants, those on a white branch only true-breeding white, while those on branches variegated in different degrees gave rise to offspring also variegated, and in similar proportions. Finally, on crossing flowers from green and white branches, plants were obtained whose colour was that of the maternal branch only, whichever way the cross was made. It must not, however, be supposed that all chlorophyll deficiencies are due merely to an absence of chloroplasts in the ovule. Genes exist which impede their development, so that green and white plants may segregate in the normal manner expressive of nuclear inheritance.

A few examples of cytoplasmic inheritance have been reported in animals. Thus, as already mentioned, the female determinant of the Gipsy Moth (*Lymantria dispar*) is held by Goldschmidt to be transmitted in this way, though the point is a disputed one. In any event, the rarity of genuine

instances of this kind serves to endorse the conclusion reached on general grounds that the cytoplasm plays but a subordinate part in heredity.

We have therefore reached the conclusion that the bulk of the hereditary factors are carried by the nuclei. Now when those of two germ-cells combine to form the first nucleus of the new individual, one of two things may happen. Either the corresponding factors may blend with one another, or they may remain permanently distinct. We shall see (Chapter X) that these two alternatives would lead to such different hereditary situations as to influence in rather a striking manner the course of organic evolution.

In all the instances which we have so far studied, the genes have retained their identity, and it may further be stated that none have come to light in which they fail to do so. On the other hand, this cannot be taken to prove that blending does not occur. It may be that the circumstances in which it is found do not readily lend themselves to experimental analysis. However, several lines of evidence are available which make such a supposition very improbable. One of them may be discussed briefly here.

If members of the same species are not identical when brought up in the same environment, then the differences between them have an hereditary basis. Suppose we cross two such individuals and inbreed their offspring, mating together brother and sister. Should the characters studied be controlled by factors which blend, then the variation would be reduced, actually it would be halved, at every generation. If, on the other hand, the factors remain distinct, their segregation will lead to a *greater* amount of variation among the grandchildren than among the children of the original cross. In making this generalization, it will be noticed that we have assumed the factors themselves to be subject to no new variation: that is to say, we have made no allowance for mutation. But we need not do so for, if the environment is constant, we cannot suppose that mutation will affect one generation rather than another. Whatever its frequency, it will be the same among the children as among the grandchildren. Consequently mutation may be neglected in considering any difference in variation which may exist between them.

It will be observed that tests of this kind are susceptible of the widest application.

They have not so far been carried out extensively, but such as have been conducted give no ground for supposing that any of the observed variation is due to factors which blend. They are, of course, capable of showing whether or not Mendelian inheritance is at work in instances too complicated to interpret in the light of ordinary experiment. These are often found, for a small addition to the number of genes which have to be studied involves a large increase in the number of segregating classes. These, therefore, become less easy to distinguish. Thus, in the absence of dominance, only two pairs of unlinked allelomorphs are needed to produce 9 classes in the F_2 generation (see pp. 43–4). Three pairs give rise to 27 classes, and even when dominance is complete 8 of these appear, segregating in a ratio of 27 : 9 : 9 : 9 : 3 : 3 : 3 : 1.[1] Consequently, when characters are under the control of several factors, the different classes may become difficult to separate when the number of allelomorphs concerned is still quite small. Should their action tend to be similar in kind but cumulative in effect, they will merge into one another very easily. This situation is extremely common, it is

[1] That is, a combination of three 3 : 1 ratios.

found especially in the control of growth (Chapters VI and VII) : a number of genes each serving to increase by a given amount the size of the whole body or of a particular part.

We may take an instance of this condition. In rabbits the ears of the Flemish Giant race average about 8 inches in length, and those of the small Polish about 4 inches. When these two breeds are crossed, the ear-length of the offspring is intermediate, averaging about 6 inches. So also are those of the F_2 generation. These show no clear-cut segregation, but include a wide range of ear-lengths between the two grandparental types. Those with intermediate lengths are the commonest, the extremes being rare. Since it is possible to arrange the individuals in an unbroken series, from those with the longest to those with the shortest ears, it may in a sense be said that the *character* (ear-length) has blended on crossing, but it is evident that it must be controlled by genes which have retained their individuality, since the ear-lengths of the F_2 generation prove to be more variable than those of their F_1 parents.

As the number of genes involved increases, so the proportion of F_2 individuals in which

the contrasted grandparental classes are recovered diminishes. In the instance just cited, ear-lengths of 8 and 4 inches very seldom reappear, indicating that the genes which control this character are fairly numerous.

Our analysis has already demonstrated two things about the factors controlling hereditary variation. First, that they are nearly always carried by the nucleus, and, secondly, that the corresponding members of a pair derived from the two parents keep their identity and do not blend with one another. But there is an evident limitation here; what of those characters whose variation we cannot study? All the features by which we judge individuals to belong to the greater divisions of animals or plants are outside the range of such investigation. We cannot examine by any direct means the inheritance of those fundamental attributes which enable us to classify a fly as an insect, a dog as a mammal, or a pea as a leguminous plant, and it has been suggested that the inheritance of these qualities is of a different kind from that controlling individual variation within a species.

There is, however, no justification for such a view as this. It is of course known

that many of the earliest developmental stages are determined before fertilization takes place. They are indeed dependent upon the cytoplasm of the egg, but this has been laid down in the presence of the maternal nuclei, themselves of biparental origin. There is therefore no need to postulate cytoplasmic inheritance for their control. The Mendelian system provides a perfectly efficient basis for this purpose, for the genes can influence the cytoplasm of the egg in the same way as that of the body-cells. These initial stages may thus be determined by the genetic constitution of the mother rather than that of the embryo.

When the hereditary control of embryonic variation has been examined, it has proved to be of the normal Mendelian type. This, of course, does not touch the fundamental problem which we have in hand. However, the analysis can be carried back a stage further by crossing forms which differ in their earliest development. Very few suitable species are available for such study. However, Tennent fertilized the eggs of the sea-urchin *Cidaris* with the spermatozoa of another form, *Lytechinus*. In the latter, development proceeds the more rapidly, and an important class of cells (those of the

' mesenchyme ') originate in a different way. In the hybrid offspring, development is purely maternal up to the time when the embryo is a hollow sphere of cells. It proceeds at the rate typical for *Cidaris*, and at this stage it has the normal appearance of that form. Subsequent development, however, including the formation of the ' mesenchyme ' cells, is intermediate between that of the two parents. I have in the past pointed out that this change in control approximately coincides with the time at which the ratio of the cytoplasm to that of the nucleus returns to normal. This is excessive at fertilization, being about fifty-seven times larger than in the ordinary body-cells, and it gradually regains its usual value (about 7 : 1 in the group under consideration) as development proceeds.

Now it seems to me probable that the nucleus cannot control a quantity of cytoplasm relatively so great as that found in the earliest embryonic stages, but that it asserts its effect when normal conditions are restored. Up to then it may well be determined by maternal genes acting upon the cytoplasm, as already suggested. Although this has not been proved, the supposition is a legitimate one, since genic action of the

kind required is, in fact, known to occur. An instance of it has already been given on p. 101, where it was explained that the direction of twist in a snail shell is determined by the genes of the parent. These affect the cytoplasm of the egg so as to control the direction of coiling adopted by the offspring.

In spite of these facts, it still remains true that we have no *direct* evidence that the most fundamental characters of the organism are controlled in the same way as those whose variation we are able to study. The task of anyone who cares to adopt the contrary view is in one sense easy. As the field of experiment is extended, demonstrating, as it has done, ever more widely the application of particulate inheritance, he can always narrow the supposed claims of cytoplasmic inheritance to influence features yet more difficult to study. On the other hand, by doing so he makes his own position increasingly untenable. It is unsound to discard a mechanism, efficient throughout as an explanation, at the particular point when it ceases for technical reasons to be demonstrable, and to substitute for it one which is of negligible importance in those situations in which its value can be assessed.

We may therefore conclude that the hereditary factors are carried in the nucleus, and that the corresponding types do not blend with one another, but preserve their identity when united in a bisexually reproducing organism. The existence of cytoplasmic inheritance in exceptional instances, provides no support for the view that the hereditary characters of organisms, whether superficial or fundamental, are controlled by means other than the particulate or Mendelian system provides.

CHAPTER VI

VARIATION

We have so far been concerned with the manner in which the genes are transmitted, and with their mutation. For this purpose we have selected one suitable effect of each, and have used this as an indicator to mark its presence. It has, indeed, been plain that the segregation of the genes has involved also that of the characters, whose different phases have appeared here and there among the stocks which we employed causing them to vary. But the variability of organisms involves far more than this. The genes in reality exert their effects in many curious ways, some serving to diminish and others to increase that general instability to which all forms of life are subject; a phenomenon which we must now study in somewhat more detail.

At the outset, it should be noticed that dominance reduces variability by masking the heterozygotes, while the existence of multiple allelomorphs increases the number

of possible types which a given locus can control. Furthermore, the total number of loci is multiplied in polyploids (p. 94), so allowing greater opportunities for variation in these forms.

On the other hand, it is not always possible to separate genes by the effects which they produce. Though perfectly distinct in their transmission, they may give rise to characters which, so far as we can judge, are exactly similar. In the Common Currant Moth (*Abraxas grossulariata*), Woodlock and Poulton have each bred pale varieties identical in appearance; both are recessive, but one is autosomal and the other sex-linked in its transmission. A somewhat similar example is provided by the inheritance of the 'rex' type of fur in the rabbit. In this form the coat is smooth and plush-like, owing to the absence, or reduction, of the stiff 'guard-hairs'. It is a condition of some commercial importance, as such skins can be employed direct by the fur-trade. They do not have to undergo the process of stripping the guard-hairs, which is normally required when soft fur has to be used. The character is recessive, and is produced by any one of three genes having similar effects. All are autosomal, but two of them are linked while

the third is carried in a different chromosome. Furthermore, in the small shrimp-like animal *Gammarus chevreuxi*, to which reference has already been made, at least six genes are known to produce red eyes. All of them are recessive to the normal black-eyed condition.

It may be inquired how factors can be proved distinct when they give rise to similar characters. In two of the instances cited, the mode of transmission clearly serves to separate them. For, in the first, one gene is sex-linked and the other not, while, in the second, though all are autosomal, two are linked but the third independent in transmission. In *Gammarus*, on the other hand, all the genes producing red eyes are autosomal, and no linkage has been detected between them. There is, however, no difficulty in demonstrating that separate genes are concerned here. So long as a single pair of allelomorphs only is involved, a mating between two red-eyed individuals will always give rise to red-eyed offspring, for the character is recessive. But if the red eye-colour of the two individuals which are mated is controlled by distinct genes, each animal will carry the normal allelomorphs of the other set. The offspring will

receive neither in the homozygous condition and, consequently, they will have *black* eyes. We may represent the genes in question as r_1 and r_2. The constitution of the parents will then be $r_1r_1R_2R_2$ (red eyes) and $R_1R_1r_2r_2$ (also red eyes), respectively. That of the F_1 generation will therefore be $R_1r_1R_2r_2$ (black eyes).

In the instances which we have just cited, the genes are not cumulative in their action. For example, the 'rex' rabbit is the same whether one, two, or three of the homozygous recessives are operating. Very frequently, however, those influencing the same character serve to reinforce one another. We have already encountered this condition in matings between large and small races of rabbits, in which it was shown that the ear-length must be due to many genes, each serving to increase it by a given amount (p. 107). Nilsson-Ehle was the first to analyse an instance of this kind. He crossed strains of wheat having red and white grains, respectively. The F_1 generation proved to be intermediate in shade, while the F_2 plants ranged from whitish to nearly full red, owing to the action of such 'multiple factors'. It is now known that they play an important part in the control of quantitative variation.

It will thus be seen that the genes may co-operate in order to produce their effects, and we must briefly examine the more important ways in which they do so. It is remarkable that some characters result from the interaction of several factors, none of which has any detectable influence without the others. Thus four homozygous recessives are required to produce brown pigment in the gold-fish. The presence of any one of their dominant allelomorphs prevents the development of this shade; the colour which the fish then assumes is controlled independently by other genes. Similarly, two 'complementary factors' bring about an abnormal condition in Asiatic cotton, causing the plants to become crumpled. We may call these *A* and *B*, and both of them, whether as heterozygotes or homozygotes, are required to produce the character in question. Neither has any effect by itself. Thus plants of the constitution *AAbb* or *aaBB* are normal and indistinguishable, but the *AaBb* plants are 'crumpled'.

Such genes as these lead us naturally to consider the important class which act as 'specific modifiers'. A large number of genetic factors appear to have no effects except in the presence of some other gene

whose influence they modify. However, the situation differs from the one just discussed, since that upon which they act does not require their co-operation in order to produce its effects. Thus a gene *s* is responsible for recessive white-spotting in mice. A further recessive, *l*, without any effect by itself, extends the spotting, which then spreads on to the face. The constitution of white-faced piebalds is *ssll*, and of dark faced ones *ssLL* or *ssLl*. Those carrying *SSll* or *Ssll* are self-coloured. Great numbers of such modifiers are known in the fruit-fly *Drosophila melanogaster*. We may quote an example. A sex-linked recessive is responsible for changing the eye-colour from a bright red to a pinkish shade called 'eosin'. An autosomal gene, also recessive, modifies this to a yellow colour without any tinge of pink, but it cannot be detected except in flies which possess an 'eosin eye'. In poultry, a gene which normally acts as an incomplete dominant produces 'frizzled feathers'. These are imperfectly formed and turned up at the ends. A simple recessive, without effect save in the frizzled condition, prevents its expression in the heterozygote, and so converts it into a completely recessive character, or nearly so. Many modifying

factors have been studied in plants. An instance of them may be drawn from the flower-colours of sweet-peas. A single pair of allelomorphs, *ee*, converts purple flowers to red, which is a recessive character. It can be modified to a salmon shade by a gene *sm*, also recessive, which has no effect on the other flower-colours. These few examples are sufficient to demonstrate the working of specific modifiers. Other instances of them will be given in the discussions which follow.

A simple extension from what has now been said will lead us to anticipate that characters may be controlled by two, or more, genes, each of which has a distinct individual effect: this expectation is realized. It is quite common to find that those controlling various characters act in a new and distinct way when brought together in the same individual. Thus in the domestic fowl, two shapes of comb, rose and pea, are both dominant to the single comb. Each is controlled by one pair of allelomorphs, which, however, interact to produce a distinct type, the walnut comb. If birds homozygous for the rose and pea comb, respectively, are mated, all their offspring have walnut combs, while walnut, rose, pea, and single combs appear in the F_2 generation segregating in a ratio of 9 : 3 : 3 : 1.

Evidently the factors concerned show no sign of linkage. In *D. melanogaster* the genes giving the recessive eye-colours brown and scarlet combine to produce white eyes, identical with those which result from the action of a single gene, distinct from either, carried in the X-chromosome. Sansome and Philp have drawn attention to an interesting example of this kind of factor interaction in the Chinese Primrose (*Primula sinensis*). The gene *W* is responsible for the production of white flowers, and *G* of a green stigma [1]. The former character is imperfectly, and the latter completely, dominant. In the presence of *G*, the constitution *WW* produces wholly white flowers, and *Ww* white with a tinge of pink round the corolla tube. However, in plants with a red stigma, *gg*, the pair *WW* allows a dark flush of colour to appear round the corolla, and *Ww* permits this to spread over the flower. The *ww* plants are always fully coloured.

The instances which we have just described illustrate that the action of a given gene can be influenced by that of another, which may or may not have a detectable effect of its own. However, a considerable number may

[1] The surface of the ovary upon which the pollen is received.

combine to modify its operation, often far too many to be analysed into their respective components. In these circumstances, it is found that the effects which a particular gene produces will be different in individuals belonging to distinct stocks or known, at any rate, to possess a somewhat different constitution. This aspect of variation is so important that we must give several illustrative examples of it.

A single pair of allelomorphs produces the recessive ' hooded ' pattern in rats, in which the head and shoulders, mid-dorsal line, and tail, are dark, while the rest of the body is white. But the character is normally very variable. Sometimes the dark pigment covers most of the body while, on the other hand, it may be restricted to the head, all the rest of the animal being white. This is due to the interaction of the gene for the hooded pattern with a considerable number of others, for these variations are inherited. The normal hooded condition is recovered when the extreme forms are crossed ; but, when individuals belonging to either of them are interbred, true-breeding strains of the dark or light type can be established.

That genes may behave in diverse ways in individuals of different constitution is also well shown by the inheritance of variegation

in the fern *Latræa atrata*. Now plants, in reality, pass through alternate generations in which the cells possess either the double set of chromosomes, as in the body-cells of most animals, or one member only of every homologous pair, as is usual in the gametes. Generally one generation is, as it were, parasitic upon the other, but in ferns both may be free-living. The condition with the double set of chromosomes is called the *sporophyte*. This constitutes the ordinary fern plant. That with the reduced chromosome number is the *gametophyte*, and in this group it forms a little green heart-shaped structure, known as a *prothallus*, which produces the germ-cells. Now the gene responsible for variegation in *L. atrata* can only affect the sporophyte, although variegation of the prothallus is inherently possible, since it occurs in other species. Thus the action of this gene depends, we might say, upon its internal environment.

In a similar way, many autosomal genes only express their effect in one of the two sexes, though transmitted equally by both. These give rise to *sex-controlled characters*. They should be distinguished carefully from the sex-linked type (p. 59), whose genes are situated in the X-chromosomes. These, of course, can influence both males and females

though, when recessive, the characters for which they are responsible appear much more commonly in the heterogametic than in the homogametic sex. Their more frequent association which the former depends upon the mechanism of their transmission ; but the restriction of the sex-controlled characters to one sex is of a purely physiological nature, and bears no relation to the distribution of the XX- and XY-chromosomes.

Three forms of the female are known in the Oriental swallow-tailed butterfly *Papilio memnon*. One, *laomedon*, somewhat resembles the male, a factor *A* converts it into the dominant form *isarcha*, while a second, *B*, interacts with *A* to produce a third form *achates*, dominant to *isarcha*. These genes, being autosomal, are inherited equally by the two sexes, but they have no effect on the males. That is to say, they can only operate in the internal environment provided by the female sex. Since *B* appears to be inactive except in the presence of *A*, it is evidently to be classed as a specific modifier of the type already discussed. Thus the constitution of *laomedon* is *aabb* or *aaB*–,[1] that of *isarcha* is

[1] A dash is used to indicate that it makes no difference which of the two allelomorphs is present as a partner, the character being a dominant one.

A–bb, and of *achates A–B–*. The corresponding males cannot be distinguished. In this instance the heterogametic sex is the one in which these sex-controlled characters are expressed. The Wood Tiger Moth (*Parasemia plataginis*), however, supplies an example of the reverse situation. In this species the yellow pigment normally present on the wings may be replaced by white; though rarely, and only in the male, which in butterflies and moths is the homogametic sex. A single factor-pair is responsible for this change. In general it may be noticed that the control of the 'secondary sexual characters' whether of the male or of the female, shows that the operation of many factors must often be dependent upon the internal environment provided by one of the sexes.

We have so far studied the genes by examining one only of the characters for which each is responsible, but it is important to remember that generally, and perhaps always, they influence the body in a variety of ways. Since they operate in controlling development, this is only to be expected. It will be convenient to give a few examples illustrating their multiple action, and then to consider it in more general terms.

The gold-fish possesses a reflecting tissue

which prevents the light from penetrating its skin. Furthermore, among the superficial cells of the body are two kinds which contain yellow and black pigment, respectively. A gene has been studied which, when homozygous, prevents the formation of the reflecting tissue. The gill-covers are then transparent, so that the blood can be seen circulating in the gills under them, while the position of certain of the internal organs may be discerned. It also prevents the development of the yellow pigment cells, and restricts those containing black pigment to a few at the base of the tail. Moreover, the iris of the eye is uncoloured in this condition. The normal fish has a coloured iris, while the reflecting tissue and both kinds of pigment cells extend over the whole body. The heterozygotes are intermediate. In the fruit-fly *Drosophila melanogaster*, a single pair of autosomal allelomorphs, recessive in effect, influences the body in two apparently unrelated ways. It changes the eye-colour from bright red to pink, and reduces the length of the wings which, in addition, often fail to expand perfectly, and remain crumpled. Furthermore, the sex-linked factor responsible for the production of white eyes in this species alters also the colour of the sheath covering

the organ in which the male germ-cells are formed (the testis), and the shape of the sac in which they are stored by the female (the spermatheca).

Very numerous instances of this kind might be given, but our purpose will be served by drawing attention to an additional fact of great importance. Nearly all the genes which have been studied affect the health, length of life, or reproductive capacity, of the individuals in which they operate. This shows us that their effects must be more numerous and far more profound than they appear superficially to be. They must, in reality, modify not only structural characters, which we can observe directly, but the general working of the body, and this in a variety of ways. Their extremely frequent, indeed almost universal, reaction upon the vigour of the organism proves beyond dispute that each one controls many characters. That those which have arisen by mutation during experimental study, or manifest themselves as occasional varieties in nature, should usually exercise their influence in a disadvantageous way, is a highly important matter which we shall discuss in Chapter VIII. For our present purpose, however, it is immaterial. It is sufficient to know

that the genes affect the life processes of the organism, so allowing us to deduce that their action is multiple and of a fundamental kind.

We are now in a position to survey the information so far collected in this chapter and to draw a general conclusion from it. We have seen that the genes interact with one another in a variety of ways, that they produce multiple effects, and that they determine both the structure and working of the body. It is clear, therefore, that the action of each cannot be considered as an isolated process. Rather they form, functionally, an interacting system which will influence the expression of every one of its members. They combine, indeed, to produce a *gene-complex* within which it is not possible to alter one component without modifying the reactions of many others. A gene may no longer produce the effects with which we are familiar when, by crossing, it has been placed in a different setting. In the Mexican top-minnow (*Platypœcilus*) a sex-linked factor $\widehat{Sp}$ merely produces dominant black spotting. In the hybrid offspring between this and another form (*Xiphophorus*) it evokes a fatal cancerous growth. Such an occurrence should hardly be a matter for surprise. True,

the genes will always produce the same effects in the same situation, that is why we can study them. But when we alter the gene-complex, and place any one of them in a new internal environment, we cannot predict the result which we shall obtain. The concept here outlined has far-reaching effects, but we must reserve a consideration of them for the later sections of this book.

Since the genes control chemical processes in the body, they interact with the external environment, as well as with one another, to produce the characters for which they are responsible. The very fact, obvious to all of us, that living organisms respond to changes in their surroundings, indicates that the action of the genes must be influenced by them. Evidently an individual is as much a product of its environment as of its heredity: the absence of one component being as unthinkable as that of the other. Although logically inescapable, and of fundamental importance in the study of variation, obvious instances in which the effects of a given gene vary in response to external conditions are not always brought to the notice of the plant- or animal-breeder at an early stage in his work. The reasons for this

are twofold. First, many genes have rather a wide toleration for environmental changes, so that a very considerable alteration may be necessary to modify their action. Secondly, all forms of life tend to maintain themselves in the particular environment which suits them best—that is to say, in a constant one : and many have rather complex adaptations to ensure this end. The implications of these two facts are of much interest, and will be considered in Chapter VIII. It will, however, be apparent that they serve to obscure, though not to annul, the fundamental response of the genes to changing conditions ; a feature of their activity which we must now briefly study.

Of all environmental changes, those in temperature are among the most important and easily examined, and they are known to affect the operation of a large number of genes. In *Gammarus chevreuxi*, a shrimp-like animal to which reference has already been made, a single pair of allelomorphs determines whether the eye-colour shall be black or red (recessive). However, the latter type becomes black-eyed when kept at a high temperature (28° C.). After some weeks in this environment, a mixed brood can hardly be separated into its two classes, so

far has the hereditary difference been obscured by the operation of external conditions (see also pp. 149–50). In *Drosophila melanogaster*, sex-linked factor affects both the development of the eye and the length of the wing, which it shortens. At 30° C. all the flies which should exhibit these characters die, though normal specimens can endure greater heat than this. As the temperature is decreased, the percentage of males and of homozygous females which manifest them falls from about 100 per cent. at 27·5° C. to 0 at 14° C. At this low temperature, therefore, the action of the gene is completely suppressed. The flowers of the Chinese Primrose (*Primula sinensis*) may, among other colours, be red or white. This difference is unifactorial, and the latter character is unaffected by temperature. The red-flowered plants, however, develop white flowers when grown in very hot surroundings. Thus above 30° C. the two types cannot be distinguished, while from 20° C. downwards the difference between them is quite clear-cut.

Since birds and mammals maintain a constant high temperature of their own, it is not to be anticipated that such effects could easily be detected in them. None the less, several examples of them are known. This

is due to the fact that the surface of the body, and particularly the extremities, lose heat so rapidly that they are not so warm as the internal organs. Now it chances that the range of temperature which affects the action of certain genes falls within that to which the exposed parts of the body may be subject. Thus in the domestic cat, the Siamese breed behaves as a simple recessive to the normal condition. Siamese kittens are whitish at birth, but their fur darkens just below the mammalian constant temperature. Consequently the coat assumes a pale fawn shade, but the extremities, which are cooler, become black. A similar state of affairs obtains in several colour varieties of the rabbit. These are the Himalayan, and two of the chinchilla shades. They are all members of a series of multiple allelomorphs containing six terms: full colour (C), dark chinchilla (c^{ch_1}), light chinchilla (c^{ch_2}), pale chinchilla (c^{ch_3}), Himalayan (c^{h}), and albino (c). The body-colour of the Himalayan is white, and of chinchilla grey (the hair contains no yellow pigment). Their extremities, however, become blackish, except in the dark chinchilla. Here it appears that the pigment is produced at a higher temperature than in the other chinchillas, or in the Himalayan

type. It seems that 'extreme dilution' in the house-mouse behaves in a similar manner. Such forms are unicolorous at birth, for up to that time the whole body has been at a constant high temperature. If kept warm in an incubator, the extremities do not darken. On the other hand, if a patch on the back be shaved, and the animals are then exposed to cold conditions, the hair which grows again is black in colour.

The foregoing instances show that temperature may affect the operation of individual genes. Its action, however, may be of a more complicated kind. Two generations of the European butterfly *Araschnia levana* are produced each year, one in the spring and the other in the summer. They are utterly different from one another. On the upper side, the spring form (*levana*) is a bright reddish-brown with black pencillings, and it much resembles the 'fritillary butterflies'. The summer brood (*prorsa*) is black with a white bar across the wings, as in the 'white admirals'. The reddish-brown form results if the pupa is cooled during a critical period of twenty-four hours after its formation; for temperature changes then act as a switch, determining which phase shall be expressed. The individual characteristics of

each are undoubtedly under hereditary control, but the environment decides which set shall develop.

It should be added that temperature influences variability in a general sense by affecting the cross-over value. The way in which it does so will be described and discussed in Chapter VIII.

Changes of other kinds in the external environment can of course modify the action of the genes. Thus a sex-linked factor obliterates the regular banding of the abdomen in *Drosophila melanogaster*. However, it operates only in moist conditions. It is usual to keep the flies in bottles containing specially prepared food for the larvæ. The perfect insects hatch over a period of some days and, as the food material becomes old and dry, the effect on the abdomen decreases until those appearing last are quite normal. However, when eggs are obtained from such individuals, their offspring show the character once more in an extreme degree if kept in moist surroundings. In the same species, a degeneration has been observed in the sac in which the spermatozoa are stored (the spermatheca). The condition proves to be unifactorial and recessive. Its expression is influenced by the amount of food available

to the larvæ: the better they are fed, the less marked is the effect of the gene.

The facts so far presented in this chapter show that variation may take place in two distinct ways. First, it may depend upon changes in the hereditary material, consisting in mutation or recombination. This is called *genetic variation.* Secondly, it may be the result of changes in the external environment: *environmental variation.*

The characters of every organism must all of them develop as an expression both of its hereditary constitution and of the environment in which it lives, but their variation may be due to one or the other component alone: though more generally both are involved. When we see that the offspring of a pair of animals or plants differ from one another, we can feel fairly confident that neither are all their corresponding pairs of allelomorphs identical, nor have they all been subjected to precisely the same environmental conditions. The variations which appear among them are consequently genetic as well as environmental.

Corresponding terms are required to describe the individuals themselves. An organism judged by its genetic constitution is

called a *genotype* : one judged by its appearance, a *phenotype*. Thus we should say that when we mate a black cock and a white hen of the Andalusian breed, the offspring are phenotypically grey (or ' blue ' as the poultry farmer would call them), and genotypically heterozygotes. It is evident that two individuals can be phenotypically similar and genotypically different. If we cross plants of the edible pea belonging to a tall and a dwarf race respectively, all the offspring are tall (as Mendel himself found). Thus the tall plant and its progeny are alike in appearance. However, they differ in constitution : the former is a homozygote and the latter are heterozygotes. On the other hand, individuals may be phenotypically similar and genotypically different : as are white-flowered and potentially red-flowered Chinese Primroses when grown at a high temperature (p 130).

Now, though variation is usually both genetic and environmental, it is possible to limit it to one or the other type. If individuals are brought up in a constant environment, any differences which exist between them must be genetic. If, on the other hand, we study a group alike in hereditary constitution, any variations which they may exhibit are wholly environmental (except for rare

mutations, which we can in no circumstances prevent). The latter proposition requires elaboration, for it may well be asked how it is possible to obtain a group of organisms in which genetic variation is absent. To this point we must give some attention.

If we inbreed a stock, mating together brother and sister, the number of pairs of allelomorphs in the heterozygous state is halved at every generation. It is not difficult to see that this is so. All those already homozygous remain so if they consist of similar types. If dissimilar, they become heterozygous in the succeeding generation. But the heterozygous allelomorphs are themselves represented as homozygous pairs in half the individuals of the next generation. This is true of every mating into which they enter, whether a heterozygote meets another heterozygote, or a homozygote. The former situation of course leads to the production of homozygotes and heterozygotes in a 1 : 1 ratio, being a back-cross. In the latter segregation in a ratio of 1 : 2 : 1 occurs, in which the heterozygotes and homozygotes are also represented in equal numbers. Consequently, it comes about that after a number of generations of such close inbreeding, say ten, the proportion of heterozygous allelomorphs

becomes negligible. The individuals so produced form what is called a *pure-line*. This is defined as a group of organisms homozygous for all their factor-pairs. It will of course be appreciated that, apart from other considerations, the existence of mutation renders a perfectly pure-line unattainable.

Now in certain species, the germ-cells develop without fertilization. When we consider living organisms as a whole, we may say that such a condition is very rare, and it appears always to be ' secondary ' to sexual reproduction. It might have been thought a transition between the asexual and the sexual types, but this is not so. The forms which arise from unfertilized eggs seem always to have had sexually reproducing ancestors in the past. For example, it is clear that the chromosomes of such eggs cannot undergo reduction, but some trace of the mechanism which normally achieves it is generally to be found in them. In species such as these, opportunities for recombination are absent and, apart from mutation, they are composed of a collection of pure-lines, irrevocably separated from one another (supposing sexual reproduction to be wholly absent, as it often is). This state is not uncommon, for instance, in a curious group

of moths, the Psychidæ, in some of which no male has ever been found. In others the males exist but are very rare, so that sexual reproduction can only take place occasionally. Every dandelion has all its factor-pairs homozygous, for the species develops without fertilization. Therefore it is split up into a system of pure-lines. If we sow the seed of a single dandelion, any differences between the members of the crop which we obtain are purely environmental. Consequently, they are not 'inherited'.

This leads us to ask what exactly we mean by inherited characters and inherited variations. Strictly speaking, the only things which are inherited are the chromosomes and the genes which they contain; these are actually *transmitted* from one generation to the next. But the characters depend on an interaction between the operation of the genes and the environment. In *Gammarus*, the allelomorphs *R* and *r* are actually transmitted from parent to offspring. The *RR* individuals normally have black eyes and *rr* have red. If we cross them, segregation in a 3 : 1 ratio occurs in the F_2 generation, which therefore varies, some of the individuals having black eyes and some red. This variation is genetic. The black-eyed and red-eyed indi-

viduals may be said to have inherited their eye-colour from the two grandparents, respectively. But if we mate two red-eyed *Gammarus* (*rr*), their offspring will all carry *rr* also. Suppose we divide them into two parts and keep one group at a high and the other at a low temperature. The brood will then vary. Half will have black eyes and half will have red. Such variation is environmental, but is the eye-colour inherited ?

In fact, when we say that a character is inherited, we mean that it reappears in a later generation. Such reappearances may indicate that it is produced by the same genes, or they may not. When we say that the genes are inherited, we mean that they are actually passed on from one generation to the next : such transmission may indicate that they will give rise to similar characters in parent and offspring, or it may not.

Logically, inheritance cannot be used with exactitude unless it be synonymous with transmission. The genes are transmitted, the characters are not. When parent and offspring have a character in common, the similarity may be environmental only. Further, they may differ sharply in some particular, yet they may even be members of a pure-line, the difference being environmental. We have

seen that the characters are always due to the genes which control them, working in a particular environment. Nearly related forms resemble one another more than those which are distantly related because they are more alike genotypically. But the effect of this is superficially enhanced by the fact that species tend to maintain themselves in a constant environment, in which the genes express themselves in the same way.

On the other hand, the general phenotypic resemblance of related forms is, on the average, an outward visible sign of a true genotypic similarity. The term heredity is understood by all and, on the whole, expresses a reality. It can hardly be discarded in the sense in which it is universally received. We may give to transmission a definite meaning, the handing on of germinal material from one generation to the next. But we may suffer inexactitude so far as to allow inheritance to cover the manifestation of similar characters in different related generations. Though in certain instances, such recurrences will be purely fortuitous, they are commonest in those forms most nearly allied. Thus, on the whole, they are an expression of genetic variation, and they may, without unduly lax terminology, be called inherited characters.

CHAPTER VII

THE ACTION OF GENETIC FACTORS

We have so far studied the genes as units transmitted from parent to offspring in the chromosomes, and the characters which they produce, as the end-products of their activity in particular environments. It will now be useful to give a brief outline of some of the methods by which the genes exert their influence on the characters. It must, however, be made clear that we can only select suitable instances for discussion, and many important considerations must altogether be omitted in a work such as this : for example, those which demand some knowledge of chemistry. Here, indeed, more than in most aspects of the subject, it is impossible to present a full and consecutive account without assuming an acquaintance with other branches of science which, of course, we shall not do.

At the outset, it is necessary to mention very briefly the problem presented by the nature of the genes themselves. This is a

subject much discussed at the present time, and one on which current views are changing. It should be remarked, however, that we have established the reality of particulate inheritance, in the sense that we know genetic variation to be controlled by units which do not blend. Consequently, it is of secondary importance what the structure of these units may be, in so far as we are concerned in working out the general principles and implications of heredity. Just as it was possible to build up a vast and accurate body of information bearing on chemical phenomena before the structure of atoms was investigated, so, though the nature of the genes presents a fundamental problem, it does not influence the conclusions which have been built upon their study, once the propositions discussed in Chapter V have been established. Now it has been supposed that the genes are distinct particles, shut off from one another in separate compartments, so to say, in linear order along the chromosomes. Furthermore, that mutations may involve any type of change affecting their structure. They may, for example, vary in chemical constitution, or suffer an actual ' loss ' of substance, partial or complete. In a sense these views are no doubt true, and we may

briefly examine them first at their face value.

It is reasonable to suppose that at times mutations involve actual losses of material. Thus a gene (ultra-white) in the X-chromosome of *Drosophila melanogaster* gives rise to several effects. It has been proved that these are also obtained when the X-chromosome breaks and that portion is lost which contains the gene. This occurrence can be demonstrated microscopically, and it has also been shown that the ultra-white effects are due not to the absence of the section as a whole but of that part of it which contains the locus of ultra-white. A word of warning may be given here. In the early years of this century, a theory known as the 'presence and absence hypothesis' was elaborated, which was supposed to explain the dominance and recessiveness of characters: the latter being thought to arise from an absence of genic material. Such a view was based upon an unwarrantable argument from characters to genes, and is certainly false. Indeed actual losses of material have been known to give semi-dominant effects. It must not be supposed that it is supported to-day in its original meaning.

It is so obvious that all mutation cannot be

due to absolute material losses, in the sense just described, as hardly to be worth stressing. The facts of reverse mutation, and the impossible evolutionary situation so reached, are sufficient to condemn such a suggestion. It may be that some multiple allelomorph series represent progressive and partial losses of material, perhaps involving a few of the molecules at a locus, which must be large in size and small in number: a suggestion which is strengthened by the fact that in forms with reduplicated chromosomes, it has sometimes been possible to build up the normal condition by bringing together a number of genes belonging to a lower stage in the series. Partial losses of material, such as these may be, do not necessarily preclude reverse mutation which, in fact, has often been detected at such loci. For it must be remembered that we are here in the presence of a 'living' system. It is undeniable that the genes 'grow', they are able to double themselves between each cell-division. A mere alteration in the relative speed of this process would be sufficient to produce a reverse mutation from a partial loss.

This brings us somewhat nearer to the true state of affairs. The recent work of Muller and others has shown that the occurrence of

mutation is specially related to breakages in the chromosomes in a manner previously unsuspected. So too it has been known for a considerable time that the genes are not in reality so isolated from one another in their activity as at first thought. The effect of a gene is *not wholly independent of its position in the* chromosome or of neighbouring breakages.

It seems clear that some mutations arise when material is lost, and that alterations in the rate of growth of genes may also produce mutation in an additive sense. Certainly we are not to regard the chromosomes as consisting of a string of isolated units. It is probably more true to say that the loci are functions of the general chemical state of the chromosome. We have seen also that chromosome mutations can either add or subtract material, providing additional loci or diminishing their number. The distinction between chromosome and gene mutations may well be one of degree rather than of kind. It is, however, necessary to stress that the view on which the genes are to be thought of as an expression at different levels of the chemical activity of the chromosomes as a whole, in no way affects their behaviour as units in particulate inheritance.

We may now consider very briefly some of

the ways in which the genes control the characters for which they are responsible. First of all, it is evident that in certain instances they manufacture substances which ooze out of the cells containing them and affect those in other parts of the body. That is to say, the action of a gene is not necessarily confined to the cell which carried it. It will be recalled that gynandromorphs generally arise by the loss of an X-chromosome in the homogametic sex. Some parts of the body are then male and other parts female. When such X-chromosomes carry an allelomorphic pair in the heterozygous state, the single X with which certain cells are left may possess that controlling the recessive character. This situation has been studied in detail in gynandromorphs of *D. melanogaster*, heterozygous for the gene producing white-eyes. It has already been mentioned that this has additional effects, for it prevents the deposition of colour in the sheath of the testis and the tube carrying the spermatozoa to the exterior. These are coloured in normal flies having red-eyes. Gynandromorphs which are male on one side of the body and female on the other, possess a testis, together with its tube, on one side of the body only. When the male

side is left with the gene for white-eyes, both the internal structures which it controls are transparent in very young individuals. However, they subsequently become coloured, as in the red-eyed form, owing to the juxtaposition of cells containing two X-chromosomes, which therefore possess the dominant allelomorphs of this gene.

In a similar way, gynandromorphs have occurred in flies heterozygous for a different sex-linked gene, that producing the recessive vermilion eye-colour (*v*). On several occasions, the chromosome abnormality has affected the head, leaving it with a single X-chromosome, carrying *v*, while the rest of the body has two X-chromosomes, with the pair *Vv*. However, the eyes of such flies were not vermilion as anticipated, owing to the existence of the dominant allelomorph *V* in the cells of other parts of the body. A corresponding result has been obtained by transplanting cells from one fly to another. The eyes of the adult are represented in the larva by small buds. These may be transferred to another larva possessing genes which affect the eye in a different way from those of the individual which supplied the graft. It may thus be seen whether the action of the one type is influenced by that

of the other. In many instances it is not, in others it is. Out of twenty-six different genes controlling eye-colour, it was found that twenty-four were unaffected in their working when surrounded by cells carrying their dominant allelomorphs. The effect of two, those for vermilion and cinnabar eye-colour, was, however, influenced by those of the host. When eye-rudiments, homozygous for the cinnabar gene were grafted into the body of a normal individual, the eyes to which the buds gave rise were of the usual red colour, instead of cinnabar. Various other examples of such interaction between genes in different cells have been detected by this means.

In individuals possessing extra chromosomes, it is evidently possible to study the effect of more than two members of an allelomorphic pair. It has then been found that the dominant condition can sometimes be reached by increasing the number of genes which give rise to a recessive character, not only in multiple allelomorphs (p. 29) but also at loci where no such series are known. In these circumstances it is evident that the differences between the members are of a quantitative kind.

We have already mentioned that genes

determine the size to which whole organisms will grow. Those which do so may have other effects, as that giving rise to the recessive condition ' vestigial-wing ' in *D. melanogaster*, which also slows down development. On the other hand, their detectable action is often limited to their influence on growth, an example being supplied by those which produce large and small races in the rabbit. In addition, genes control the *rate* at which processes proceed in the body, and the time of their onset. This aspect of their operation is so important that we must consider a few illustrations of it.

The eye-colour of *Gammarus chevreuxi* may either be black, the normal condition, or red, the recessive one. Furthermore, the red-eyed form slowly develops black eyes at high temperatures as already explained. We may now analyse this situation in more detail. The eggs of this species are laid in a brood-pouch where they hatch, and in which the young are carried for a day or two by the female before they are liberated. If the development of the normal black-eyed form be followed, it is found that the eyes are at first bright red. However, they darken during a period of a day or two, through shades of brown and chocolate to black, a

stage which they have nearly reached at the time the young are extruded. This is due to a black pigment, *melanin*, which is laid down in the eyes in increasing quantities until the red coloration is completely obscured. Now the eyes of the red-eyed form also darken, but very gradually, until they reach a chocolate shade in old age. It has been found that this is due to the deposition of a small quantity of the same black pigment. It takes place so slowly that a change which occupies a few hours only in the normal form requires, in ordinary circumstances, many months to accomplish in that with red eyes. In both types, the rate at which the black pigment is produced increases as the temperature rises. When kept at 28° C., the young of the normal form are born with eyes completely black. At 23° C. they are dark chocolate in hue for a day or two, and at 14° C. they are at first distinctly red. In the red-eyed animals, practically no darkening ever occurs at 14° C. ; at 23° C. the eyes become brown after some months, and at 28° C. they are blackish after three weeks. It is now clear that the allelomorphs concerned, *R* and *r*, do not merely produce black or red eyes as such. They control the rate at which a single substance, melanin, is

deposited, the *rr* constitution retarding the process very greatly.

It will be recalled that the genes controlling sex in insects determine the rate of the male and female developmental processes, and the time at which one type is superseded by the other. Furthermore, in the Gipsy Moth (*Lymantria dispar*) Goldschmidt has shown that the Eurasian larvæ are dark in colour, while those from south-western Japan are light. This difference is due to the action of a single pair of allelomorphs. The heterozygotes are intermediate when young, but when older they become as dark as those of the pure Eurasian form. It seems that these genes influence the rate at which pigment is deposited in the body. In the dark larvæ, they operate so early that even the young are heavily pigmented, while in the light race they act so slowly that a sufficient amount of pigment is never formed during development. The allelomorphs act quantitatively, so that the process proceeds with intermediate speed in the heterozygotes. It does so too in the race from the north of Japan, in which the larvæ are at first light and darken later. This is due to a multiple allelomorph.

The destruction of the black and yellow pigment cells which takes place in the gold-

fish is determined by an allelomorphic pair which control the rate of this process. They lead to a series of colour changes during the life of the fish. These take place in a regular order: brown, brown variegated with orange, orange, orange variegated with white and, finally, white with no trace of orange. In the heterozygotes they occur with intermediate speed. Several genes are known which determine the rate of feathering in birds; also the development of structures in mammals, as that which influences simultaneously ear-length and skull-length in the mouse.

Genes acting in a similar way are also important in plants, and here one aspect of their operation deserves special notice. The gametophyte generation (p. 122), possessing the single set of chromosomes, is greatly reduced in the flowering forms. In the male, it consists of the pollen-grains, and these have to grow down the stigma of the flower in order to reach the female gametophyte, which encloses the eggs. Consequently, the genes which control the rate of growth of the male gametophyte may lead to departures from expectation in the ratios of segregating families; for the slower-growing pollen tubes will less often effect

fertilization than those which grow more rapidly. Thus in maize, a single allelomorphic pair is responsible for the waxy condition, recessive to the non-waxy. The gene producing the former type also slows down the growth of the male gametophyte, so that waxy plants are less common than expected in those families where both forms are present.

It appears, then, that genes often affect the speed at which processes take place in the body. Now as an organism grows, certain relations are maintained between the sizes of its parts; these have been analysed in detail by J. S. Huxley (1932). A study of their components throws further light upon the operation of the genes which influence them.

Suppose y is the size (let us say the weight) of a particular organ, and x that of the rest of the body, minus that of the organ in question. Then the relation of the organ to the body throughout growth is given by the formula.

$$y = bx^{\alpha}$$

in which b and α are constants. The term b merely expresses the initial relationship: that is to say, the value of y when $x = 1$. However, that of the exponent is of great

interest. When $\alpha = 1$, the size of the organ remains the same relative to that of the body. When $\alpha > 1$ it increases, and when $\alpha < 1$ it diminishes. If the value of α is much above or below unity, a given increase in the size of the body produces a very disproportionate change in that of the organ. Now genes may influence one or other of these components. The fruit of the gourd *Cucurbita* can assume very different shapes, owing to differences in the relation between its length and its diameter. These are under the control of two pairs of allelomorphs, which interact to produce the various forms. Since the proportions of the fruit are established at the earliest stages of development and alter but little during growth, these genes are primarily concerned in establishing the value of b in the formula. However, in the pepper plant (*Capsicum*), the shape of the ovary remains practically unaltered until about the time of fertilization. The proportions of the fruit then gradually change until the various forms characteristic of the mature pod are attained. These are genetic, and it is clear that the genes which influence them do so by determining the value of α in the same formula.

We must now leave the phenomena of growth, and turn our attention to other

aspects of genic action. Very striking advances have taken place during recent years in our knowledge of the ' ductless glands '. Now a gland is a structure which manufactures substances of use in the body, and its products are normally carried to the place where they are required by a tube called a ' duct '. Thus the liver makes a substance, bile, which is of value in digestion, and this is brought to the intestine by the bile-duct. On the other hand, it has been discovered that certain organs, once thought functionless, are in reality glands which pass the substances which they manufacture into the blood flowing through them. They are, therefore, ductless glands, and very small quantities of their products are required to bring about profound changes in the body. Genes which influence the development of the ductless glands therefore produce important effects upon the whole organism.

For example, a single allelomorphic pair produces dwarfing in the mouse, the condition being recessive. This it does by affecting the action of one part of the pituitary body, a ductless gland which lies below the brain. The dwarfs cease to grow at an early stage and only reach about one-third of the ordinary weight. When, however, pituitary bodies

from normal individuals are grafted into the dwarfs, they attain almost to the full size. It is evident therefore that the gene which produces dwarfing acts by affecting the pituitary gland, and that it does not influence growth in other ways.

Another ductless gland of great importance is the thyroid. It is situated in the neck, and in man its enlargement gives rise to goitre, while an individual who suffers from a deficiency of its product becomes a dwarf imbecile of the type called a cretin. It has been found that the coastal and desert races of the mouse *Peromyscus maniculatus* differ markedly in the structure of their thyroid glands: so much so that sections of them can easily be identified as belonging to one or the other. We do not know how this difference is controlled. It may be genetic or, on the other hand, the gland may have to assume distinct forms in order to produce the necessary amount of substance in the coastal and desert environments. However, it no doubt plays an important part in the life of the two races.

The genes whose action has been most thoroughly studied are those which control colour in plants and animals. A great deal of information has been obtained on the

chemistry of pigments, and much is known of the reactions which occur when these vary genotypically or phenotypically. Unfortunately, this subject is too technical for treatment here. One or two points in connection with it may, however, be mentioned briefly.

In animals, the stages by which the genes control the 'melanin' pigments have been rather fully investigated. These pass through a series of colour-changes, from yellow, through shades of red and brown, before becoming blackish, which is their final condition. They are responsible for most of such colours in animals. The genes determine at what point the reaction shall cease and, consequently, the tint ultimately to be assumed. The various coat-colours of mammals, and the body-colours of *Drosophila* are members of such a series.

These melanin pigments are among those which colour the butterflies and moths, but various others are also employed by these insects. Some of them are allied to uric acid, which is an excretory product of animals, and they are responsible for white, yellow, and red shades. Many species, as the Tiger moths, have alternative red and yellow forms under simple hereditary control, the pigments involved being of this type. It appears prob-

able that the genes which produce the yellow colour, which is nearly always recessive, stop short a reaction which, when carried to completion, would give the red shade. White and yellow pigments of quite another type are also found in butterflies. These are derived from the plants upon which the larvæ feed, and comprise the *flavones* and their chemical allies (p. 159). I know of one instance in which white or yellow of these two different kinds is used by alternative forms of the same species; most unfortunately, the control of this remarkable situation has not been studied.

The butterflies and moths nearly always carry their pigments in little scales attached to the wings (and body). These can be rubbed off as a coloured dust, leaving the wing-membrane transparent. The complex patterns of these insects are determined by a double process which involves accurate timing. The pigments are produced in the body at intervals determined by the genes interacting with the environment. However, the scales are formed at varying rates, controlled in a similar fashion, and only those which have reached a particular phase of development can take up the pigment which floods the wings during their forma-

tion. If the undeveloped wing of a butterfly be removed from the pupa, its pattern can be seen faintly indicated in monochrome, marked out by the scales which have reached different stages. In this way, the various colours are limited to particular areas on the wing, while they and their distribution are controlled by the hereditary constitution of the organism and are subject, in addition, to environmental variation.

The work of Scott-Moncrieff and others has resulted in a remarkable advance in our knowledge of the chemistry of plant pigments. They have studied, in great detail and in a variety of forms, the reactions which occur when the colours are modified by different genes. For our purpose, these pigments may be grouped under three main headings. First, the water-insoluble type carried by the plastids (p. 249) : these include chlorophyll and carotin, and they are discussed more fully on p. 160 ; a number of genes are known to govern their production. Secondly, the anthoxanthins (flavones and flavonols) : these are soluble in the sap, and vary in colour from a pale ivory shade to very deep yellow. Thirdly, the anthocyanins, pigments also soluble in the sap, provide a series of colours from scarlet, through shades of purple and

violet, to clear blue. The two latter groups are very large. The chemistry of many members of them is known, and numerous genes have been studied whose operation determines which of them shall be produced.

In addition, certain genes control the acidity of the cell-sap. They therefore modify the colour of some of the pigments, which then act as ' indicators ' in the same way that litmus turns red or blue in acid or alkaline solutions. Thus in the Poppy (*Papaver Rhœas*) a gene *P* makes the cell-sap more acid as compared with its allelomorph *p*. The flowers, which are red in the former condition, become purple in the more alkaline plants.

Finally, we may mention examples of those instances in which the genes modify the process of digestion. They thereby affect the characters of the organism, since they limit the materials available for the use of the body. The green colour of plants is due to a pigment, *chlorophyll*, which, in reality, is composed of two related compounds. These are chlorophyll-A, of a blue-green shade, and chlorophyll-B, which is yellowish-green. Associated with them are two other substances: yellow *xanthophyll*, and orange-red *carotin*. In the North Ameri-

can Clouded Yellow Butterfly, the larva, the pupa, and the eyes of the perfect insect are normally grass-green in colour, due to the presence of these pigments. They are obtained direct from the leguminous plants upon which the larvæ feed. However, a gene, recessive in effect, prevents the digestion of all save the chlorophyll-A. The various structures coloured in this way therefore assume the blue-green hue of that compound. Even the eggs are affected, being white in this variety, for the substances are absent which normally colour them yellow.

A gene which acts in a somewhat similar manner produces most interesting effects in *Gammarus chevreuxi*. This species belongs to the Crustacea, a group which includes the shrimps, crabs, lobsters, and allied forms. They are generally pigmented by carotin, one of the compounds to which reference has just been made. Now it is probable that animals are unable to manufacture this substance for themselves. They obtain it either from the plants which they eat, or from other animals, themselves vegetable feeders. Carotin can exist in another form beside the red one already mentioned ; this is bluish or greenish in hue. It can easily be converted into the red phase by alcohol

or by heat: a change with which we are familiar when a lobster is boiled. In *Gammarus*, as in most Crustacea, the body is pigmented with greenish carotin. However, this is converted into the other form in the eye, where it is responsible for the red coloration to which reference has already been made. It will be recalled that it is present even in the black-eyed form in which, however, it is hidden by melanin, except in early development. The latter pigment is of quite a different nature, and is manufactured by the animal itself.

Now a mutant form has appeared in *Gammarus* in which the greenish body-colour is absent, leaving it chalky white. The eyes of this variety are normally black, but if the individuals possess the genes (*rr*) which slow down the deposition of melanin, they are colourless, instead of red—as expected. This condition, known as 'white-body', is recessive, and controlled by a single factor-pair ($\widehat{wbwb}$). Evidently it results from an absence of carotin in both its phases, the green type from the body and the red from the eye. The production of melanin is unaffected, since this substance bears no relation to carotin.

It is extremely interesting to analyse how the gene in question prevents pigmentation by carotin, and so produces the characters by which we recognize its presence. Though autosomal in transmission, its effects are related to sex in a curious way. In studying them, it is advisable to use the potentially red-eyed form, since the effect upon the eye can then be detected in addition. If we mate a ' white-body ' female ($\widehat{wbwb}$) with a normal male heterozygous for the gene ($\widehat{WBwb}$), segregation in a 1 : 1 ratio should occur, half of the offspring will be of the ' white-body ' form and half will be normal (though heterozygous). When the young are extruded, it is found, however, that they are all of the ' white-body ' type ; but half of them become normal after they begin to feed. The reason for this is clear when it is understood that the eggs of the normal form contain a large quantity of green carotin, so much that they appear almost black. Those of the ' white-body ' form contain none and are white, for the females have no supply of carotin with which to provide them. It is evident that the store of green carotin in the egg furnishes the young with sufficient of this substance, which they can-

not manufacture for themselves, until they can obtain it from their food.

Now does the gene for ' white-body ' prevent the digestion or the utilization of carotin ? The reverse cross is capable of deciding this question. If we mate a ' white-body ' male ($\widehat{wbwb}$) with a normal but heterozygous female ($\widehat{WBwb}$), half of the offspring should once more be of each type. But all are normal on extrusion. In half, however, the colour in the body and eye fades during growth, and these become ' white-body ' individuals. Since the female parent is normal, she can provide her eggs with carotin. The fact that all the young are normal at first, shows that those with the gene for ' white-body ' can use this substance if supplied with it. That half of them lose their pigmentation subsequently, shows that they can obtain no further stock of it. It is clear, therefore, that the action of this gene is restricted to preventing the digestion of carotin, and to this fact all the peculiarities of the ' white-body ' form are due.

Theoretically, it should be possible to produce ' white-body ' environmentally, by feeding normal *Gammarus* upon a carotin-

free diet. However, certain technical difficulties are encountered in this procedure. The experiment has never succeeded in my hands, and I am in doubt if it has ever been satisfactorily performed.

From the brief survey presented in this chapter, it will be apparent that the genes may exert their influence in very various ways, and indeed they do so at all stages of development. It need cause us no surprise, therefore, that their effects are susceptible to changes in the environment, whether external or internal.

CHAPTER VIII

SELECTION

THE mere fact that Darwin was the first to study the effects of natural selection is probably known to most of us. Before following them ourselves, we must consider briefly what the idea of selection involves. Certain individuals may be chosen as the parents of the succeeding generation and, if any of their characters are inherited, the choice will influence the type of offspring produced. Now the 'selection' of individuals here involved may be carried out artificially, by human agency, or naturally, by the environment. The plant or animal breeder may desire to establish certain qualities in his stocks, and he deliberately breeds from the individuals which exhibit them, instead of allowing random mating to take place. In natural surroundings, those which possess the most advantageous qualities, being the best equipped for life, will succeed most often in reproducing their kind. They will therefore

contribute more to posterity than their less fortunate contemporaries.

Now at the outset it is evident that effective selection cannot take place in a stock which does not vary. Where all individuals are alike, choice, in the widest sense, can only be fortuitous. Furthermore, selection will have no effect in altering the qualities of a stock unless the characters upon which it operates are inherited. Whatever agencies may be at work in conserving some and rejecting others, no permanent change can be produced if their variation is purely environmental. This fact is indeed self-evident, but it can be put to the test by selecting within a pure-line. Here all variations, apart from rare mutations, are environmental. Johannsen selected for seed-weight and other characters in a species of bean. By using the largest and smallest beans from a mixed stock, he was able to produce strains differing very considerably in the weight of their seed. Since the species is normally self-fertilized, *each plant* is, however, a member of a pure-line. He found that individuals raised from the largest and smallest of its seed did not differ in the average weight of the beans which they produced. That is to say, he

could not alter the constitution of a pure-line by selection. In plants in which cross-fertilization is taking place, some of the variation in seed-size is due to segregation in the genes controlling it. Consequently, by sowing the heavier and the lighter seeds, lines differing in seed-weight can be produced, for selection has now operated on genetic variation.

In this chapter we shall discuss the effects of selection, whatever the agency exercising choice may be. That the process is efficacious when deliberately practised by the plant or animal breeder, there can be no doubt. He may work upon characters controlled by single genes or by many, but by constantly picking out for reproduction specimens possessing the qualities he requires, he will establish a stock containing the genes which evoke them; a fact which can easily be shown by experiment, as in the instance just cited. It may, however, be questioned if we can demonstrate the reality of *natural* selection. Are certain inherited characters favoured, and others eliminated, in nature? Not only does a vast amount of indirect evidence confirm such a view but, in a number of instances, it has been established by direct proof. It

will be interesting to give an example of such a test.

Gordon released 36,000 specimens of *Drosophila melanogaster* on an estate near Totnes, in South Devon. The flies carried the gene for the recessive body-colour *ebony* ($\widehat{eb}$) and its normal allelomorph ($\widehat{EB}$) in equal numbers, for the three genotypes $\widehat{EB}\widehat{EB}$, $\widehat{EB}\widehat{eb}$ and $\widehat{eb}\widehat{eb}$ were distributed in a 1 : 2 : 1 ratio among them. At the end of the summer, 120 days after release, the flies were trapped, and the proportions of the two allelomorphs were ascertained by breeding. That of the ebony gene had fallen from 50 per cent. to 11 per cent. during this period, which would represent about five or six generations. Such a result can be explained in two ways. Either selection had operated against the $\widehat{eb}$ gene, the normal wild-type condition being at an advantage, or else the population had been diluted by other normal individuals. Now the latter alternative can be excluded. The species is not indigenous in England, and any specimens which occur are brought into the country with imported fruit. The proportion of the $\widehat{eb}$ gene was found to be the

same in flies captured in different parts of the estate. This included a food store, the focus from which any imported specimens would have spread. Had these been introduced in significant numbers, they would certainly have been especially common here : consequently, the $\widehat{eb}$ gene would have been disproportionately rare in flies found round the store, which it was proved not to be. It is clear, therefore, that natural selection had operated in favour of the normal condition, and that the elimination of the ebony type had, in fact, been very stringent.

It is evident that selection tends to preserve certain genetic variations and to reject others. It must therefore reduce the variability of the species. Indeed, we may justly regard genetic variation as in equilibrium between mutation and recombination tending to increase it, and selection tending to diminish it. In fact, many instances might be cited which demonstrate that variation increases in situations in which the severity of selection is reduced.

Certain butterflies are believed to derive protection by their close resemblance to others which birds, and enemies of various kinds, find inedible owing to their nauseous taste. A resemblance of this kind is called

'mimicry'. Those which practise it may depart very widely from the group to which they belong, in order to copy a distasteful species which acts as their 'model'. Such 'mimics' very frequently assume a number of distinct forms, generally under simple hereditary control (pp. 183–5), each resembling a particular model. A series of different modifications, often along surprisingly diverse lines, are then necessary in order to achieve a set of sufficiently convincing resemblances. Though the various forms of a mimic may be so distinct, each one of them is generally extremely invariable; for selection eliminates those which depart from the requisite appearance. However, it happens in special circumstances that a mimic may extend its range into districts where its models are rare or absent. In these circumstances, its various forms no longer remain constant.

A very large random collection of butterflies made near Entebbe, at the source of the Nile, included 111 specimens of the well-known African mimetic butterfly *Papilio dardanus*, in several of its forms, and 1,949 specimens of the species which they copy. A similar random collection was made at Nairobi, in the mountains east of Lake Victoria. Here *P. dardanus* is quite com-

mon, and 133 specimens were included in the captures.[1] However, its models were rare in this mountain region, only 32 of them being obtained. Now in the former sample, 4 specimens (3·6 per cent.) of the mimic belonged to forms in which the pattern is imperfectly developed, so that they depart from the appearance of the various models. In the latter, 42 (32 per cent.) were imperfect in their resemblance. These figures show that in the race from Entebbe, the models are 70 times commoner relative to their mimics, and the imperfectly developed forms of the mimic are 8 times rarer than in that from Nairobi. The variation of the mimic, which supervenes in the district where the models are no longer common enough to provide it with much protection, provides a striking example of the fact that selection tends to maintain uniformity.

The reproductive capacity of any species may be taken as large enough to balance the elimination to which its offspring are normally subject. Consequently, it is always far in excess of that required to maintain its numbers at a constant level, if all were

[1] Only the females are included in the totals of *P. dardanus*, since the males do not mimic.

to survive. Should they do so, a condition would soon be reached in which they could not find sufficient food. In the absence of variation, survival will be at random. Normally, however, it is 'selective', those best fitted to their environment tending to be preserved. It is evident, therefore, that selection acts as a check upon numerical increase. Should its effects suddenly be diminished, a species will generally multiply until its numbers are held back at a higher level. But we have just seen that a reduction in selective intensity has another effect: it promotes variation. Consequently a rapid increase in numbers is often associated also with increased variability.

For example, an isolated colony of the Marsh Fritillary Butterfly (*Melitæa aurinia*), was studied over a total period of fifty-five years. From 1881 to 1897 the species was extremely common, but from that year onwards to 1919, its numbers declined until it became very rare. Throughout the whole of this period the individuals were decidedly invariable. However, for the next five years an extraordinary outburst of variation coincided with a rapid increase in numbers, so that by 1924 it had once more become abundant. From that time onwards the level

of the population remained stationary, and marked variation ceased. Yet the constant form which was then attained differed in certain particulars from that which characterized the colony before the period of variation set in.

Now such a fluctuation in numbers as this, is not an isolated occurrence. Elton has shown that the populations of animals and plants are subject to occasional, and often regular, numerical changes of an extreme nature, and it is clear that they provide opportunities for modification. There must be a number of gene-combinations available to most species which do not differ greatly in survival value, though they may indeed adapt the organism in different ways. These have been compared by Sewell Wright to peaks, separated by valleys representing intermediate combinations less advantageous in nature. Normally it is difficult for selection to shift the species across a valley from one favourable type to another. But when the intensity of selection is mitigated and variation increases, many of the less satisfactory combinations can be realized, so that the species may cross to other peaks upon which it will be cut off from further change by the occurrence of stricter selection. In

support of this view, it is very noteworthy that most of the more extreme varieties encountered during the period of rapid increase in the *Melitæa* colony were actually deformed, the degree of their imperfection being roughly proportional to the extent of their departure from the normal form. Such varieties as these would have been unlikely to survive in ordinary circumstances.

Since mutation is a random process, it will nearly always lead to changes of a disadvantageous kind. We have seen that the genes are functionally related to one another, so that they form an interacting gene-complex within which one component cannot be changed without affecting the others. On the other hand, selection has preserved those characters which are favourable. These are maintained genetically by a delicately adjusted system, whose balance a random change is far more likely to upset than to improve. So too with variation due to recombination. We have already seen that two genes when brought together in the same individual may produce effects distinct from those to which either alone gives rise. Their nature is largely unpredictable. It must, in addition, be

noticed that recombination will influence the adjustment of the gene-complex in the same general way as mutation. In short, genetic variation is far more likely to produce disadvantageous than favourable characters.

With this fact in mind, we may return to a consideration of selection. We have seen that it tends to produce uniformity and, on the other hand, that it is ineffective in the absence of genetic variation. Unless a species possesses a great reserve of such variability, selection will be unable to adapt it to changing conditions and to new environments. So long as a species is able to vary, it may survive: if it is without that capacity, it can never hope to persist in a changing world. This is the chief function of bisexual reproduction. As a mere source of new individuals, a non-sexual process is far superior: fewer risks are involved. But the advantage of the bisexual method is related not to reproduction as such, but to the maintenance of genetic variability, whence its extraordinarily widespread occurrence among both animals and plants.

This leads us to envisage a somewhat curious state of affairs. Since the genes interact with external conditions to produce

the results for which they are responsible, there must exist for every organism an environment which suits it best. This we call its *optimum*, and all individuals should endeavour to remain as near to it as possible. This they do by migrating to the best conditions, by carrying their own optimum environment about with them (as do the birds and mammals, which always live at the temperature most favourable for them), and by a variety of other means.

Now when an organism is in optimum conditions, random variations are most unlikely to be advantageous. As it departs from them, it becomes rather more probable that among such changes may be found one which improves its reaction to the environment; while if the organism is in very unfavourable conditions, such as are liable to prove fatal, almost any change is worth trying, 'in the hope' that it may improve the situation. In fact it would be a most desirable state of affairs for organisms to vary less at their optimum than in other environments. There is some indication that they do so.

A microscopic animal called *Paramecium*, so small that its body is not divided up into cells, lives readily in stagnant water

in which grass is decaying. If we keep creatures in optimum conditions, each individual usually reproduces simply by dividing into two. Such an act allows no opportunity for recombination, and the animals remain invariable. If we do not renew the liquid in which they live, their excretory products poison it, and the nutriment becomes exhausted, until they are in danger of extinction. As the conditions depart from the optimum, a bisexual method of reproduction, rare before, becomes common. The offspring now vary. The forms which they assume are random, in the sense that none is specifically adapted to suit the new conditions, but there is a chance that one among them may be better fitted to them than was the original stock. This type would then be preserved by natural selection. Such random variation would not be worth while when all is well with the culture.

It is possible that we find an expression of the same state of affairs in more highly organized forms. It has already been mentioned that the cross-over value, like other manifestations of genetic variability, can be modified by the environment. Now it is evident that the fundamental effect of crossing-over is to increase variability, for

without it genes in the same chromosome could not be recombined. In *Drosophila melanogaster*, the cross-over value has in certain instances been found to vary with the temperature in a curious way. The percentage of recombination is high both at high and low temperatures, and low at intermediate ones. Thus, if we plot the cross-over value against temperature, we obtain a U-shaped curve. It is perhaps not without significance that the optimum range of temperature for this fly (about 22°–24° C.) is at the bottom of the U, so that it is the one at which the insect is least variable. Genes which affect crossing-over are quite well known, and it may be that selection has favoured those promoting it in conditions which depart from the optimum in either direction.

We have so far thought of selection as operating in approximately the same way as Darwin himself had conceived. That is to say, the agent at work, whether it be the plant or animal breeder, or the natural environment, picks upon certain of the genetic variations which present themselves and preserves them, rejecting others. Looked at in this way, selection is merely concerned in incorporating in a stock those

genes which produce desirable results. But there is another side to this picture. The fact that the genes interact with one another to give rise to the characters, indicates that it may be possible for selection not only to retain one and discard another, but to modify their *effects*. The process is, in a sense, able to do more than merely to select from what is provided : it may improve upon the action of the genes which it uses, or diminish the harmful influence of others whose presence the species has to suffer.

This possibility may have occurred to the reader, for an example of it has already been given him. It will be remembered that the effect of the single allelomorphic pair producing the recessive hooded pattern in rats can be modified by selection, so that true-breeding and distinct strains can be established within this one character (p. 121). This result has been obtained by human agency, and examples of the same phenomenon might be given in large numbers. We will choose for further analysis one in which the selection is performed by the environment, though taking place in artificial conditions in which it can be studied in detail.

In *D. melanogaster*, a single pair of autosomal genes produces a recessive ' eyeless '

condition, in which the eyes are minute or absent. In addition, such flies are weakly, being shorter lived, and laying fewer eggs than normal. We may mate two eyeless flies and inbreed their offspring for a few generations, say five or six (which can be produced in a few weeks). Since the character is recessive, all will be homozygous for the gene concerned, but they do not long remain eyeless. In successive generations, flies with larger eyes appear, at the same time they become more hardy and, by the end of the experiment they are scarcely to be distinguished from the normal type. It is clear that one of two things must have happened. Either the eyeless gene itself has changed, and done so gradually since the modification is not sudden, or else the response of the flies to the eyeless gene has altered. It is easy to decide between these possibilities. We may take our modified eyeless flies, cross them to the normal type, and re-obtain the recessives in one quarter of the F_2 generation. If the gene itself had been influenced its effects would be modified still: but they are not. Flies exhibiting the eyeless condition to its full extent now appear, showing that it was the reaction of the stock to this particular

gene which had changed. Therefore, when replaced in the wild-type constitution, it produced its original results.

It is now clear what has occurred. The flies when first mated would possess many genes in the heterozygous state, and their segregation would produce genetic variation. With the forms so arising, the eyeless gene would interact in different ways. Those combinations which tend to suppress its disadvantageous effects would be favoured, and the individuals in which they occurred would leave most descendants. In this way, selection would modify the eyeless character, though the gene which controls it remains unaltered.

A similar change in the effects of the genes may certainly be brought about by selection in nature. The existence of such a process serves to explain certain phenomena which were obscure until its operation had been recognized. We may take as an example one group of instances in which it appears important.

Reference has already been made to the principle of mimicry in butterflies. It involves certain curious features which merit attention here. Relatively unprotected species often copy a number of different models,

or forms of the same model. It is evident that a powerful advantage accrues from so doing. For their numbers cannot be increased so much that a particular conspicuous pattern comes to be associated by their enemies more with something edible than with something of repellent flavour. Clearly, the numbers of a mimic are limited by those of each mode lwhich it can resemble. The various changes necessary to bring about a convincing likeness may affect many characters : colour, pattern, shape, and habit. Some or all of them may be involved when two or more forms are copied. Yet it is repeatedly found that a single gene converts one set into another.

In East Africa, two forms of the butterfly *Hypolimnas dubius* differ from one another in colour, pattern, and habit, in order that each may mimic a distinct species. Yet they are controlled by one pair of allelomorphs. As already explained, a single gene (*B*) converts one form, *isarcha*, of *Papilio memnon* into another, *achates*. The latter mimics a distinct species (*P. coon*). This is a tailed butterfly, but *P. memnon* is normally without tails. They have to be produced as one of the characters evoked by this gene, together with modifications in

colour and pattern: otherwise the resemblance would be imperfect.

The action of single genes then may modify a species in a variety of ways each involving an accurate resemblance. But the genes arise suddenly, by mutation. Are we really to think that selection has had to wait for the occurrence of mutations which shall produce fortuitously all the distinct characters required? Such a piece of good fortune would be almost incredible were it to occur once only, but the situation is a common one. Pure luck of this kind cannot provide the basis upon which selection operates. It has been suggested that the various resemblances are due to 'parallel mutation' in model and mimic. That is to say, the same gene has been thought to exist in each, its changes producing the same series of effects in both of them; just as the albino characters (white coat and pink eyes) may be, and probably are, due to a parallel mutation in the rabbit and rat. But in mimetic butterflies such a suggestion cannot possibly stand the test of critical examination, for here the resemblances are generally purely superficial: such as deceive the eye and no more. Similar colours are produced by chemically different

pigments, and the approximation in shape is often a skilful illusion. The genes concerned in model and mimic cannot possibly be the same.

It seems that the explanation of this remarkable state of affairs has already been provided. A mutation in one species will sometimes chance to produce some resemblance to another, and better protected, form. This will be subject to genetic variation, due to segregation within the gene-complex. Those varieties which tend to improve the resemblance will be preserved by selection, as will be the constitution which gives rise to them. In this way the mimicry will be achieved *gradually*, but will remain under the influence of a single gene which can act as a switch in maintaining alternative forms. This must have arisen spontaneously by mutation, but we are not therefore to suppose that the mimicry which it controls did so too, in all its perfection.

Here, in the mimetic butterflies, we often find that several distinct forms of a species are maintained together in the same habitat. However, this condition, known as polymorphism, occurs in many other situations. The term must be limited to those instances

in which the different forms remain in stable equilibrium. Where one is spreading through a locality and replacing another, we are concerned with a transition only, and the problems which relate to polymorphism do not arise. These result from the maintenance side by side of different forms in definite proportions. Now in order to reach this state of affairs, two conditions have to be fulfilled. First, the action of selection is a necessity. A gene whose effects on survival are neutral (if such exists), can be shown mathematically to spread through a species only with extreme slowness. The period of time required for it to affect a considerable proportion of a large population would generally be fantastically great. Secondly, though selection is therefore a prerequisite for polymorphism, this condition cannot arise except where the selective advantages of the different forms are balanced one against the other. If one of them is simply more favourable than another, it will spread completely through the species. Two or more forms can only coexist permanently where the advantage enjoyed by one wanes, vanishes, and is converted into a disadvantage, as its numbers increase relatively to the others.

There are two ways in which the spread of a favourable character may be checked in this manner. The first is environmental, the advantage actually being lost as the numbers increase. This is true, for instance, in mimicry, where, as already pointed out, a resemblance to a distasteful species can only be useful up to a certain point, after which it becomes a danger: when the pattern in question is too often associated with edible instead of inedible qualities. The balance in numbers between the two sexes is another, and most striking, example of this kind. The second method is genetic. If a heterozygote is at a greater advantage than either homozygote, polymorphism must result. We know that many genes have harmful effects, and we shall see that these are generally recessive (pp. 188–9). When a gene beneficial in its results is closely linked with one of them, the advantageous characters which it produces can only be realized in the heterozygous condition: so that polymorphism ensues. The white female form of the American Clouded Yellow butterfly (*Colias philodice*) is prevented from replacing that of the more normal yellow colour, over which it has some advantage, owing to linkage of this kind.

We are now in a position to gather up and unify several of the conclusions which we have reached independently. Mutations, we have found, far more often lead to unfavourable than to advantageous changes. Also they recur continually, though very infrequently. Furthermore, we shall see that when a gene is rare, it must be present immensely more often in the heterozygous than in the homozygous state (pp. 201–3). We have established the fact too that the effects of the genes may be modified by selection.

Now when a mutation occurs, selection will favour those combinations which tend to modify the effects of the gene to which it gives rise in a favourable way. If, as is usual, these are disadvantageous, that constitution will spread through the species which evokes them to the least extent; as in the eyeless condition of *D. melanogaster* already cited. Further, this will be restricted almost entirely to their heterozygous manifestation. There will be a constant tendency, therefore, for the effects of disadvantageous genes to be suppressed in this state. That is to say, for them to become recessive. Such a process will be exceedingly slow, but the recurrent nature

of mutation allows it to be fairly persistent. It has been calculated that the time required for it is not unreasonably great. If, on the other hand, a gene produces such disastrous results that the individuals which possess it rarely leave descendants, the species will have little opportunity to adjust its reaction to them. We might expect therefore that they would remain of intermediate expression in the heterozygote, and such they generally prove to be.

Those rare mutations which produce genes having beneficial results will evidently be subject to the reverse procedure. The constitution which expresses them most fully will be favoured, so that their influence will be magnified in the heterozygote, and they will become dominant. Since they tend to be preserved, this process will be very rapid compared with the drift towards recessiveness of the disadvantageous type.

It will be apparent that the quality of dominance is not fortuitous : that it is produced by selection, and that the recessives represent disadvantageous types. These important conclusions have been reached by the brilliant analysis of R. A. Fisher. They are open to experimental verification, which has substantiated them.

If the effects of genes have really been modified to become recessive, owing to selection suppressing them in the heterozygous condition in nature, it should be possible to achieve the same result artificially. Further, by placing recessives in gene-complexes to which they are not accustomed, their heterozygous effects should once more be obtained. We have already encountered an instance in which one gene can convert the effects of another from the semi-dominant to the almost completely recessive state (p. 118). Many more instances of this kind are known; we may mention one of them. The European Buff Ermine Moth (*Spilosoma lubricipeda*), which is yellowish in colour, has a remarkable chocolate-brown variety (*zatima*), seemingly first encountered in Heligoland. It is due to the action of a single factor-pair, the heterozygotes being intermediate. By selecting in opposite directions, Federley was able to obtain strains in which the variety had gone far to becoming a complete dominant or a complete recessive, respectively.

The various members of a multiple allelomorph series will constantly be balanced against their normal allelomorphs in ordinary circumstances. As each is very rare, they

will never meet in nature, so that the species has no experience of the reaction which two produce simultaneously. Consequently, we find that every member of such a series is recessive to the wild-type condition, but that two of them, when brought together artificially, have intermediate effects.

If dominance and recessiveness were functions of the genes themselves, rather than of the response of the internal environment to them, they should be invariable qualities. That they are not so is now well known. The larva of one of the Chocolate-tip Moths (*Pygæra anachoreta*) normally possesses a pair of white spots, which are absent in a recessive variety. That of an allied species (*P. curtula*) always lacks these spots. In the hybrid between it and (spotted) *anachoreta*, the spots are present but imperfect. The dominance of the gene has become incomplete when it has to act in a gene-complex half of which has not been selected to produce it. It is interesting to notice that this fact appeared so curious when it was first reported in 1911 that the observation was doubted. This was before the theory of dominance-modification had been advanced: to-day, however, its significance is clear.

Similar results have been obtained by crossing races and species of plants. Thus the variety crinkled-dwarf behaves as a recessive in Sea-island Cotton. But it ceases to do so in the descendants of a cross between that species and those races of Upland Cotton in which the mutation has not occurred. The heterozygotes are then intermediate. Fisher himself has studied the effect of several dominant genes in poultry, when acting in the gene-complex of the wild jungle-fowl; the species from which the domesticated breeds are derived. He held that dominance had been produced by artificial selection favouring the more striking forms, and that it would be lost in the unmodified internal environment provided by the original race. This view proved to be correct. Among those studied, the behaviour of the gene producing the crest of the Japanese Silky fowl was particularly interesting. It is a dominant character. In the wild jungle fowl it evoked an entirely new effect when homozygous. This was a 'cerebral hernia', bursting the brain upwards between the bones of the skull. This dangerous defect was completely recessive in the wild birds, though that merely raising the feathers on the head

into a tuft had not become so. Artificial selection had carried these results further, completely suppressing the hernia even in the homozygous condition, but the crest had been retained and enlarged as a curiosity.

It is evident that dominance and recessiveness could not be produced by selection acting on the gene-complex unless many of the allelomorphs are heterozygous in natural conditions. The absence of factorial blending ensures this, while the genes controlling recessive characters are preserved from extermination when in the heterozygous state. However, it has now been proved experimentally that much genotypic variation exists in natural populations.

J. B. S. Haldane has suggested another means by which selection may produce dominance. As already mentioned (Chapter VI), the members of a multiple allelomorph series tend to act quantitatively. Furthermore, they will often manufacture substances up to a ' saturation level ', which represents all that the individual requires ; production beyond this point is superfluous. Now selection will favour those members of such a series which elaborate a sufficiency of material even in single dose, that is in the heterozygous state, although the amount

will be unnecessarily great in the homozygotes. This will give a dominant effect. The operation of the disadvantageous lower members of the series, whose activity is deficient, will be obscured except when they are present in double dose: that is, they become recessive. It will be noticed that this concept necessitates that the progress of a character towards dominance is accompanied by the selection of *different genes*. However, the instances which have been examined experimentally generally show that the gene itself is *not* affected: it is the response of the organism to the gene which is changed. Though no doubt responsible for it in certain instances, it therefore appears likely that dominance is more frequently reached by the means suggested by Fisher.

It is clear, then, that dominance is a purely phenotypic effect. Such expressions as a 'recessive gene', so frequent in the literature, give a misleading impression and, strictly, ought not to be used: for dominance and recessiveness is not a property of genes but of characters. It will now be realized that selection, whether conducted artificially or by natural agencies, is important both in preserving useful genes and in modifying their effects.

CHAPTER IX

PRACTICAL APPLICATIONS, AND HUMAN HEREDITY

THE plant or animal breeder may desire to know how best he can improve his stocks, fix in them desirable qualities, or obtain new variations which shall supply him with fresh material. We may briefly consider the methods which he can adopt.

From time to time a character worth preserving as useful or curious may appear among domesticated or wild forms. If controlled by a single allelomorphic pair, no difficulty should be experienced in utilizing it. Should the character be dominant, the gene determining it will be in the heterozygous state. This will almost invariably be true, whether it has appeared in cultivation, and presumably therefore by mutation, or whether it has been found in nature. Only normal individuals will be available with which to mate the variety, so that half the offspring obtained will possess the desired character. Should it be recessive, it will of

course appear in one quarter of the F_2 generation. When, however, it is possible to obtain a back-cross between an F_1 specimen and the abnormal parent, this is certainly to be preferred ; for one-half, instead of one-quarter, of the offspring then possess the desired character. If, on the other hand, a number of genes are concerned in its production, these will be scattered by segregation at the first mating with the normal form. They can, however, be concentrated again by interbreeding the offspring. As already explained (p. 136), this procedure reduces the proportion of heterozygotes, so that the different homozygous types crystallize out, as it were. Continued selection of those in which the desirable character is most fully expressed, will not only produce its maximum effect, as the greatest number of genes controlling it are brought together, but will fix it in the homozygous condition.

These facts are really self-evident. They have been mentioned to indicate that the first stage in incorporating a new variety ought to involve close inbreeding. This is a procedure which may be regarded with considerable misgiving. The impression that it is generally harmful is indeed reflected by the marriage laws of most countries, and will

be endorsed by most of those who have practical experience in breeding animals, if not plants. Furthermore, it will be realized that the type of inbreeding here required is of the closest kind : a series of brother and sister matings, or a back-cross to a parent. Now the bad repute which such a method has gained is not wholly deserved. We must consider the basis upon which it rests.

It has already been made clear that recessive characters are disadvantageous. Evidently the genes which produce them are sheltered from selection in the state in which they generally exist ; that is to say, the heterozygous one. Every bisexually reproducing organism therefore possesses a large stock of genes capable of giving rise to disadvantageous variation, which is realized here and there as they chance to be brought together in homozygous pairs. By inbreeding, this tendency is increased. Consequently, the unfavourable qualities which the organism may be capable of producing are unmasked. But if the individuals which exhibit them are rejected, the stock is actually purged of such genes, and left only with their dominant allelomorphs. Close inbreeding need not therefore be ultimately harmful : rather it is beneficial when practised in

combination with strict selection. The initial loss which the occurrence and rejection of the homozygous recessives involves may, however, prove a serious item when the larger and more valuable domestic animals are inbred.

We see therefore that inbreeding combined with selection can raise the quality of the stock, which is thus purified from those genes which produce disadvantageous results. Furthermore, inbreeding also provides a valuable source from which curious or even useful variations may be obtained. Great numbers of the rarer varieties found in animals and plants are really due to the occasional manifestation of recessive characters whose genes are by no means uncommon in the heterozygous condition (pp. 201–3). The collector, it may be of butterflies and moths, or the horticulturist, possesses the means, rarely used, of tapping this great reserve. By breeding from wild specimens and *raising the F_2 generation*, it is extremely likely that interesting material will be procured. It should be remembered that this procedure should be strictly followed. If a number of wild individuals are used, the offspring of each must be interbred, as a mating between brother and sister, to produce the succeeding generation, which is the one

likely to yield striking results. At the same time, valuable information may be gained on the amount of heterozygosity in the wild population, the kinds of variation which it can produce, and other matters. Nor must it be thought that the forms so obtained are necessarily useless. These varieties have become recessive because they are disadvantageous *in natural conditions*, but they may not be so under domestication. The individuals possessing many of the qualities most prized by the agriculturist and stock-breeder would certainly be eliminated in nature.

That is one source of variation. It consists in concentrating the genes which give rise to the rarer forms. A second method depends rather upon obtaining new combinations, which normally may never be realized. This may be achieved not only by combining in the same individual two rare varieties which would not meet otherwise, but by crossing widely separated races or distinct stocks. It will of course be realized that such a course may involve something more than bringing together desirable qualities which have been separately attained. Since the genes interact to produce their effects, new characters, possessed by neither parental race, may appear among their hybrid des-

cendants. This is particularly true when distinct species are interbred; for very different gene-complexes will have been built up in them. But their progeny will too often be sterile for this type of mating to be usefully adopted, even where attainable, except in rare circumstances. However, a single 'out-cross' between distinct strains may provide much variation, from among which the most favourable forms should be chosen and inbred with rigorous selection. True-breeding stocks possessing desirable qualities can be established in this way. It will be evident that the task of the plant breeder will be greatly simplified by his power to take cuttings. A useful form can be perpetuated by this means, without enduring the hazards of segregation.

It will be evident that gene-mutation cannot normally be relied upon to supply a source of new forms. The process is far too rare and too difficult to accelerate. Variations in chromosome number can sometimes be made to provide the plant, but not the animal breeder, with valuable new material as indicated in Chapter IV. Their effects will also be further discussed on pp. 225–6.

We have just mentioned that when a recessive character is rare, the gene control-

ling it may none the less be quite common in the heterozygous state. This leads us to inquire into the important question of the proportions in which the genes may be expected to occur in populations breeding at random. Most of the interesting problems so raised are beyond the scope of this book, but it will be useful to discuss one or two of the simplest of them.

Since a pair of allelomorphs, autosomally transmitted, can exist in three phases—as homozygous dominants, heterozygotes, and homozygous recessives—six types of mating are possible between them. Now the proportions to which each gives rise are fixed by the ordinary rules of segregation. Furthermore, the number of loci available for an autosomal gene is normally twice that of the number of individuals in the population. With these facts in mind, it is not difficult to see that, however many of them a given gene may occupy, the three classes will occur in definite proportions and in stable equilibrium.

Indeed, it can easily be shown mathematically that at whatever proportion of its loci a given autosomal gene may exist, that particular value remains fixed until some extraneous agency, such as selection, disturbs it. Such stability is reached in a

single generation. Furthermore, it can, as anticipated, also be proved that, at whatever level of abundance this stability is attained, the proportions of the three classes always bear a simple relationship to one another. That is to say, the number of individuals belonging to the heterozygous class is twice the product of the square roots of those forming the two homozygous classes. Thus if the number of individuals in the homozygous dominant class (D) is p, and if in the homozygous recessive class (R) it is q, that in the heterozygous class (H) is easily found. For the three classes D, H, and R are distributed in the ratio

$$p : 2\sqrt{pq} : q$$

or, more conveniently,

$$p^2 : 2pq : q^2.$$

It is clear therefore that if we know the number of individuals in any two classes, that in the third can readily be calculated. Furthermore, even when dominance is complete, so long as we know the proportion of recessives in the population, we have only to solve a quadratic equation in order to find the proportions in which the other two types are distributed.

This is a most important fact. It is often

extremely useful to be able to determine how many individuals in a population are heterozygotes for a given gene, and to make calculations of a similar nature. It may be helpful to give an example. Suppose the white-flowered variety of a plant is found to be a simple recessive to that with coloured flowers. In a field where it is common, we find that 5 per cent. of the plants bear white flowers. What proportion of those having coloured flowers are heterozygotes? The two first terms of the above ratio together equal 95. Therefore

$$p^2 + 4{\cdot}47p = 95$$

so that

$$2p = 15{\cdot}53.$$

The three classes D, H, and R, are accordingly distributed in the ratio

$$60{\cdot}3 : 34{\cdot}7 : 5.$$

Slightly more than one-third of the plants bearing coloured flowers are heterozygous for the gene in question.

Suppose that the character had been a dominant one. In these circumstances, most of the plants with white flowers will be heterozygotes. How rare, in reality, are the homozygous whites? The reader should find no difficulty in discovering that, out of the whole population, approximately only one plant in fifteen-hundred (1 : 1,537) will be of this type.

Such calculations will sometimes enable us to draw deductions in regard to the hereditary control of a character where actual breeding experiments might be difficult or costly. Here we can only mention an instance of the simplest kind. Suppose it is suggested that three forms of a species, *A*, *B*, and *C*, are determined by a single allelomorphic pair of genes. Such a tentative conclusion might have been reached by a study of the pattern, supported by the fact that when one of the rarer types has been found, the other has always been present in addition. Let us assume that we examine the species in its natural environment and, on capturing 100 specimens, we find that 10 are of form *C*, 20 are of form *B*, and 70 are of form *A*. Now, having captured 10 per cent. of the rarest type, we should expect 43·24 per cent. of the population to be heterozygotes. Those of intermediate frequency, presumed to be such, are therefore considerably too rare: we only obtained 20 of them. The chances against such a deficit are very heavy (actually, of course, they can be calculated [1]). Indeed, these figures make

[1] The methods for doing so are explained by R. A. Fisher in his admirable book, *Statistical Methods for Research Workers* (Oliver and Boyd). This provides

it extremely improbable that the three forms are, in fact, related in the simple manner suggested.

Assuming that they are genetic, our result may be accounted for in three possible ways. First, the hereditary control may be of a more complicated kind. Secondly, it may be that the types do not mate at random. This is an unlikely, but not unknown, situation. Thus the Five-spot Burnet Moth (*Zygæna trifolii*) produces a very rare black variety, which is a simple recessive. It was found that the individuals preferred mating with the form unlike themselves (normal males tend to select black females, and the reverse). Thirdly, the three classes may not be equally hardy: one may survive more often than another. From what has been said on polymorphism (p. 187), it will be apparent that when such a situation as this exists, it is likely that the heterozygote will be at an advantage over the less common homozygote. This should lead to an excess of type *B* in our example. Actually, this was the type which was too rare. Consequently, in the particular circumstances which we have chosen, our result strongly

the necessary information for the treatment of mathematical problems in heredity.

indicates that the three forms are not controlled by a single allelomorphic pair of genes.

It is evident, therefore, that the ratio which we have considered will not be attained in practice if the three types are not equally hardy. It should also be remembered that it applies only to autosomal genes. Sex-linkage involves a somewhat different situation, into which we cannot enter here.

Such indirect methods as those just discussed are the only ones available for the investigation of human heredity. Indeed, the human species provides the worst possible material for the study of inheritance, for this is an experimental subject. We are immensely handicapped when our only resources consist in the mathematical analysis of existing populations and in the examination of pedigrees, often inaccurate and generally omitting the information which should provide us with crucial evidence. None the less, a large number of inherited characters have been successfully studied in man. It would, however, be most inappropriate to include any list of them in this book, which is concerned with principles only. It will therefore suffice to draw attention to a few special points and general conclusions which arise from a survey of them.

It is important to realize that the transmission and operation of the genes is fundamentally the same in our species as in others. Indeed, by a study of rare sex-linked conditions, Haldane has even been able to secure information on the mutation rate in man. It seems to be approximately the same in the fly *Drosophila*, though probably slightly greater.

It does appear, however, that human sex-linkage presents some rather curious, though not abnormal, features. As there are twenty-four pairs of chromosomes in man, all of approximately equal size, it might be expected that by far the greatest number of genes to be discovered would be autosomal. Yet a very considerable proportion of them have, in fact, proved to be sex-linked. Now at first sight, this is not a particularly striking fact, for this type is much the more readily detected : since all sex-linked genes exercise their effects in the heterogametic sex while, as we know, autosomal recessives rarely do so in either. However, a comparison with other Mammals, the group to which the human species belongs, shows us that we are faced with a real distinction here. Very large numbers of genes have been studied in other members of this Class. In particular,

in the Rodents, including such forms as rats, mice, rabbits, and guinea-pigs ; the Carnivores, such as cats and dogs ; also in the Ungulates, or hoofed animals, to which the horses, cattle, sheep, and swine belong. Among all of these, no single instance of sex-linkage has ever been detected, except for the gene producing yellow coat-colour in cats. Man evidently differs in this respect from his allies ; in them, perhaps, the X-chromosome may be largely occupied by those genes directing sex-control, so excluding those whose operation is of a more general character. Yet this is not the normal condition. Sex-linked genes not directly related to sex-control are generally quite numerous as, indeed, we know them to be in birds. It is the other mammals which are exceptional, not man. Furthermore, man occupies a peculiar place among those of his class whose heredity has so far been studied ; for he has departed less than they from the ancestral type from which all are descended. Except for those modifications associated more or less closely with the development of his marvellous mental powers, man by no means represents the ' highest form ' of a mammal. He retains many features possessed by the ancestors of the other forms,

which they themselves have lost or modified : and, as pointed out by Haldane, one of these is to be found in their X-chromosome constitution. In his abundance of sex-linked genes, man departs from the special characteristics of his group, and resembles more those forms from which it is derived.

Another striking feature to which Haldane has also drawn attention consists in the existence of a certain amount of crossing over between the human X- and Y-chromosomes. The X-chromosome may be regarded as composed of two sections. One possesses substance identical with that of the Y-chromosome, with which it pairs and exchanges material during germ-cell formation. The other is distinct, and remains permanently isolated from Y. In man, genes are known in both regions, for the former is of considerable size. Sex-linkage is not therefore as sharply separated from the autosomal type as in some forms. For if the interchange which takes place between X and Y were quite unhampered, which it is not, a gene in this region would behave as if autosomal. It may well be that such ' partial sex-linkage ' is commoner than is generally supposed, for it is not easy to detect.

As in other forms, the genes whose

transmission has been traced in the human species manifest their presence in a variety of ways. Some influence relatively unimportant characters, such as eye-colour. This is under the major control of a single pair of allelomorphs, the blue and grey shades being recessive to brown: so that simple segregation generally results, and the offspring of two blue-eyed, or grey-eyed, parents do not include brown-eyed individuals. However, other genes affect it in a subsidiary manner, leading to exceptions in inheritance and to intermediate conditions. Genes are also known which operate in a quantitative manner, as those responsible for the control of human height. However, limited as our methods of study are bound to be, most of our knowledge relates to disease; its actual inheritance or the susceptibility to acquire it. For this subject is the one on which information is most easily obtained; indeed, it is often the only one available in an examination of pedigrees.

Now a number of diseases are controlled by a single gene. Some are sex-linked, as the Hesse Disease already described (pp. 59–61), and others are autosomal; some are dominant in their effects, and others recessive. Most of those producing more serious consequences

are rare, for there is heavy selection against them : the individuals suffering from them often failing to reproduce. They are none the less important, not only for the patients themselves but for the members of those families in which they are known to be transmitted. Some of the dominants do not give rise to marked symptoms early in life, while the recessives rarely or never do so when their genes are in the heterozygous state. Those who belong to such families may desire to know whether they carry these genes. The simple facts of segregation indicate that they may chance to possess their normal allelomorphs, when their hereditary constitution is perfectly sound. On the other hand, they may be heterozygotes. In that event, are they justified in marrying and transmitting the taint to their descendants ? In particular, a woman who comes of a family in which there exists such a sex-linked recessive may require to know whether, were she to marry, half her sons will suffer from the disease and half her daughters transmit it, or whether they will be perfectly normal and healthy. At present we are not in a position to give this information, but we need not despair of being able to do so. If our knowledge of linkage in man were more

complete, half as complete as in *Drosophila*, for instance, it would generally be possible to state that the chances are very considerable —or very remote—that such individuals are in fact heterozygotes. Great numbers of observable characters must really be inherited in a simple manner. A study of their association with one another, and with such dangerous conditions, would provide us with the facts we require.

It is very desirable, therefore, to establish the linkage relations of inherited characters in man. Not only are observable structural traits, such as hair-colour and the shape of the features, available for this purpose, but so are a number of less apparent qualities. The blood of all human beings can be divided into four groups, which determine the safety with which it can be transfused. Blood from one individual may be injected into another if he belongs to the same groups as himself or, sometimes, to one or more of the other groups. If, however, the wrong group is chosen, the corpuscles [1] of the injected blood are agglutinated: that is, they clump together, with dangerous or fatal results. Fortunately it is quite easy to

[1] Blood consists of cells, called 'corpuscles', floating in a liquid, the 'plasma'.

find out in advance if this will happen, by mixing a few drops of blood from the intended donor and recipient, and watching the result under the microscope. The agglutination, if it occurs, is then easily detected.

Now these four blood-groups are controlled by a series of three genes, two being dominant and the third recessive in effect. Since they are multiple allelomorphs, not more than two of them can be present simultaneously. One group, *AB*, is produced by the presence of both dominants, the second, *A*, by that of one dominant alone, and the third, *B*, by that of the other, while the fourth group, *O*, is the recessive one. The proportions in which they occur are characteristic of different races, but the *AB* group is the rarest. If blood tests were conducted on a number of those families in which hereditary diseases occur, it would be possible to ascertain whether the genes controlling them are carried in the same chromosome as these multiple allelomorphs.

The blood of human beings can also be classified by means of its reaction to that of other animals. Evidence is accumulating to show that the differences encountered here are genetic. It may therefore be possible to map the position of a large number of the

genes scattered along the human chromosomes. This would allow the linkage relations of most hereditary conditions to be detected, the importance of which will now be apparent to the reader.

A curious effect discovered a few years ago can be used in linkage tests in a similar way. About one-quarter of the population are unable to taste an organic compound called phenol-thio-urea, and some of its chemical allies. This is intensely bitter to those who can detect it : so at least I am informed, for I am unable to do so myself. The ability to taste it is a dominant character controlled by a single gene. In addition to their use in linkage tests, both this and the blood-group genes may be of value in settling doubtful paternity. For example, it is evident that the children of two ' non-tasters ' must resemble their parents in this character, since it is a recessive one. Of course these genes are liable to mutation, but so rarely that legal decisions are constantly, and quite properly, accepted when the possibility of error is far greater than this involves.

There can be no doubt that mental, as well as physical, disorders are inherited. The constant recurrence of feeble-mindedness in the same families even when their members

may be brought up in widely differing environments, leaves no room for doubt that the condition is inherited, often on quite simple lines. The marriage of two feeble-minded persons produces with great frequency a family of feeble-minded children. So often indeed that we may feel confident that the character is often recessive and controlled by a single pair of allelomorphs. On the other hand, this interpretation is far too simple to cover all the instances and, indeed, this is what we should expect. The character is a complex one, and must certainly be produced in a variety of ways. Undoubtedly a number of different genes are involved, some dominant in their expression, others recessive, and some intermediate. However, as already mentioned, a simple recessive type is certainly often encountered.

It is plain therefore that the marriage of the feeble-minded is strongly to be discouraged. In particular, that of two feeble-minded persons is extremely liable to result in a mentally defective family. Although its exact basis is often in doubt, the inheritance of this and other mental disorders is susceptible of definite proof by the use of correlation (p. 99). By this means it can be shown that the frequency of such characters

among relations exceeds their distribution in the population as a whole by an amount which cannot be due to chance.

The method of correlation is of course susceptible of wider application : it demonstrates that various kinds of mental ability are inherited. Such qualities are exceedingly difficult to analyse and, from their nature, we may expect that many genes are involved in their control. However, the inheritance in certain families of the more striking mental attributes cannot be denied. The system of intelligence tests which has been elaborated, allows the lower levels to be graded : utterly incapable, though I believe them to be, of assessing the higher mental types. However, the application of correlation to results obtained in this way, certainly suggests that the genetic component is represented in the variation of mental and moral qualities to a degree differing not widely from that of physical characters. Such studies, together with those of Lidbetter and others indicating the inheritance of the tendency to crime and vagrancy, even when all allowance is made for the environment, demonstrate the fallacy of the view that all individuals would be equal were they to be granted equal opportunities.

CHAPTER X

EVOLUTION

IT is no longer seriously denied that organic evolution has taken place. That is to say, organisms have become modified in the process of time, so that an individual may bear little resemblance to its remote ancestors. Forms wholly distinct to-day may be traced back to a common origin and, as we now know, two different species may occasionally combine to form one. Space cannot be allowed in a book on Heredity to present even a summary of the overwhelming evidence which demonstrates the reality of evolution. However, there is still much controversy over the means by which it has been achieved, and it is essential to indicate how the facts which we have discussed bear upon this problem.

We have already seen that mutation must usually be disadvantageous (p. 175). When, however, it does chance to produce a favourable character, the gene to which it gives rise will spread through the species and

become incorporated in the wild-type gene-complex, save in the special circumstances of polymorphism (pp. 185–7). Except where the advantage is exceedingly minute, this process will take place fairly rapidly. Consequently, such a gene will not long remain a ' mutant '. That producing the former ' wild-type ' character, which it displaces, will become its recessive allelomorph. If, therefore, the mutations which we encounter in experimental work really represent the type of change which is employed in evolutionary progress, we should expect to find that they will very seldom produce effects which could be of use to the species. Their failure to do so has been entirely misunderstood by many authors, who have therefore thought that they cannot represent the source from which the variation used in evolution is derived. True, they seldom produce changes which could be of the slightest value in nature, but we should not expect them to do so !

Just occasionally, however, mutations producing a considerable effect appear to be of some potential advantage to the species. I judge that this would be an almost impossible occurrence if the environment were constant. Had the advantage been real in the

past, the recurrent nature of mutation would have ensured that such genes would long ago have been incorporated in the species as a whole. Since the environment is not constant, what was of no advantage in former times may be useful to-day. We may here pause in our argument briefly to consider a few illustrative examples.

The Florida Velvet Bean which can normally only be grown in the Gulf States of America produced a mutant form capable of surviving in a more varied environment. Furthermore, the extraordinary change which has affected moths in industrial areas during the last eighty years is particularly relevant to our present purpose. Within living memory, certain species have become black in manufacturing districts, though they have retained their original coloration elsewhere. This has happened repeatedly, and the condition appears always to be under a simple hereditary control, being dominant or semi-dominant and generally determined by a single gene. Where data are available, it appears that the black specimens are actually hardier than the typical forms. In spite of this, they have entirely failed to spread outside industrial areas though, in certain instances, they have been known to occur as rarities in un-

polluted country. I have elsewhere suggested that those genes which produce advantageous effects, combined with the deposition of black pigment, have failed to spread owing to selection operating against this colour. For these forms are decidedly conspicuous where the normal ones are well concealed. However, in industrial districts, where the countryside is frequently blackened by smoke, and their enemies are rarer, these species may be able to take advantage of the other useful effects of such genes, whose influence on pigmentation may be no longer a handicap. Here, I believe, we have examples of genes which have been able to spread owing to a change in the environment.

It should be noticed also that the combination for two recessive and disadvantageous genes may be superior to either alone. That producing the recessive character 'arc' (modifying the wing-shape) reduces the average length of life of *Drosophila melanogaster* from thirty-nine to twenty-seven days. That giving rise to purple-eyes, also recessive, is yet more harmful, reducing it to twenty-six days. However, the individuals possessing both these characters survive for an average of thirty-four days. Furthermore, the presence of two mutant

genes may sometimes restore the wild-type condition, as do those in *D. melanogaster* producing the characters 'facet' (affecting the formation of the eye) and facet-notched (modifying the wing-tips). They are multiple allelomorphs and, when present together, return the specimens to normal. Several similar instances are known. Such combinations might occasionally produce a real improvement.

We may now continue our argument. Though, as we see, it is not impossible that occasional changes of detectable magnitude may prove advantageous, we may fairly conclude that those genes which produce minute effects, interfering least with the existing balance, will be the type most often beneficial. R. A. Fisher has lately drawn attention to the fact that some evidence for the spread of genes having such minute advantages can, in fact, be obtained. He points out that mutations producing genes approximately neutral from the point of view of survival must be exceedingly rare and, from what we know of mutation, they must be supplied to all species at approximately the same absolute rate. Now when owing to a change in environment one of these becomes slightly advantageous, it will spread. In

doing so the ratio between it and its allelomorph will gradually reach equality, yielding an increase in variation. As the proportion of the new gene surpasses that of the old, the observed variability of the population will decline again. Now common species may be able to maintain more genes spreading through the population than can rare ones. This will be due to their ability to keep in reserve more of such genes having neutral effects, and owing to the larger number of individuals exposed to the chance of excessively rare advantageous mutations. Any difference which may exist between the variation of more and of less abundant species will therefore be due to that fraction of the variation by which evolutionary progress is actually taking place. It has now been established that such differences in variability between abundant and rare species do, in reality, exist ; so demonstrating the spread of genes possessing minute advantages. In addition, it must not be forgotten that their effects will be enhanced by selection as they become common, in the manner indicated in Chapter VIII.

It will be evident that for this process, as for the accomplishment of some of the selective changes already discussed, long periods

of time will be required : and, indeed, long periods are available. It is not generally appreciated how great is the length of time occupied even by relatively small evolutionary changes. The forms of life existing in past ages can be studied from their fossil remains preserved in the rocks. However, these represent a very small fraction only of the period during which life has existed upon the earth. Nearly all the fossils laid down in rocks earlier than those belonging to the so-called Cambrian age have been destroyed. We can trace to that epoch many of the existing groups. They become progressively modified as we follow them backwards : but, generally, their more fundamental features have been fully established in the most ancient specimens which have been preserved. Of the evolutionary stages which preceded them we have no direct knowledge.

It is instructive to ascertain how long has been available for that portion of evolutionary progress which has taken place since the deposits were formed which gave rise to the first Cambrian rocks. The coal which we burn in our fires is formed from the remains of those forests which flourished half-way between that time and our own, or a little earlier. This was from 260 million

to 300 million years ago, and our ancestors were then newt-like creatures which had not long begun to colonize dry land : for originally they were purely aquatic. The first of the Cambrian rocks are another 200 million years or so older, and when they were deposited our own ancestors resembled extremely primitive fishes. The length of time, about 500 million years, which has elapsed since then is difficult to visualize, but I am indebted to Professor J. S. Huxley for a striking analogy which provides us with a basis upon which to judge it. Suppose that the thickness of a single sheet of typewriting paper be taken to represent one hundred years. Then the pile of paper which would be equivalent to the time since the beginning of the Cambrian period would be one thousand feet high, equal to the height of the Eiffel Tower. The time since the most recent glacial period, when England was last covered with ice, would be represented only by one foot of paper, while the length of recorded history would be equal to a little packet of two or three dozen sheets.

It must not, however, be thought that all minor evolutionary changes are slow. Indeed, we have seen that a changing

environment may allow genes to sweep through a considerable section of the population in quite a short period of time : forty or fifty generations in the moths of industrial areas, to which reference has already been made. Furthermore, polyploidy may give rise to distinct changes in a single generation. It has been pointed out in Chapter IV that polyploid forms, though unimportant in animals, are by no means rare in plants. They have certainly played a considerable part in the minor evolution of that group.

Of special significance in this connection are the allotetraploids, for they may be quite fertile forms, though sterile with the two species from which they are derived. Nor must it be thought that they are necessarily mere intermediates between them. The gene-complex of each has become sufficiently distinct to prevent the chromosomes from pairing when brought together, and may produce factor-interaction giving rise to characters present in neither diploid. Some of these will occasionally confer an advantage on their possessor.

There are a number of instances in which the occurrence of allotetraploidy in nature can be traced. An excellent example is provided by the rice-grass *Spartina Town-*

sendii. This has spread from the neighbourhood of Southampton Water, where it appeared somewhere about 1870. It is true-breeding, but is almost certainly a hybrid between the English *S. stricta* and the American *S. alterniflora*, (with both of which it is sterile). These have 56 and 70 chromosomes, respectively, while *S. Townsendii* has 126. It has no doubt arisen as an allotetraploid, the two parental haploid numbers of 28 and 35 having doubled in a hybrid individual. Some of its characters have certainly given it an advantage over the native form. We have good reason to think, therefore, that hybridization may be an important factor in the evolution of plant, if not of animal, species.

It was explained in Chapter V that we have no reason to think that factors which blend play any considerable part in the control of heredity. Here we differ radically from Darwin, who worked out his theory of natural selection on the assumption of blending inheritance. The evolutionary difficulties to which such a view leads have been analysed with great skill by R. A. Fisher. We must briefly consider them.

If the hereditary factors of an organism

were to blend,[1] then the genetic variability must be halved at every generation. This necessitates either that the genetic variability, upon which selection alone can operate, must be very rare, or else it must be maintained by mutations. If these are sufficient to balance the effects of blending inheritance, they must be very common indeed. Since it is clear that bisexually reproducing animals do, in fact, possess very considerable genetic variability, Darwin was forced to accept the latter alternative. The fact that pure-lines do not, might have warned him that his assumptions were incorrect; for such a high mutation-rate should sustain their variability also. Since the alternative possibility, that of particulate inheritance, did not occur to him, he was driven to certain contradictory conclusions. First, as the effect of blending must be corrected by mutation, half the genetic variability of every individual must be supplied by this means in every generation. Consequently, nearly all the variation upon which selection can work must be of very recent origin. In addition, the advantage possessed by any selected character must be so considerable

[1] It may be mentioned that Darwin did not distinguish between genetic and environmental variation.

that it can be spread through the population in a very short time, before it has been 'swamped' by intercrossing. That these two deductions are false, there can be little doubt that Darwin himself realized. His own studies had shown him that, on the whole, evolution involves slow changes of small magnitude. However, they induced him to attach much importance to agents controlling or directing the production of new variation (that is, of mutation), which indeed would be just if they were to supply half the hereditary variation of each individual. But the mutation rate necessary to maintain particulate inheritance is exceedingly minute. Agents which control it are therefore very unimportant in determining the general course of evolution. With blending inheritance, a doubling of the mutation rate would produce an immense effect; with particulate inheritance, its influence is small indeed.

It will thus be seen that the importance of any evolutionary mechanism which depends upon modifying the flow of mutation must be negligible compared with that attached to it by Darwin. One of these consists in the supposed transmission from parent to offspring of characters newly acquired by

the individual during its lifetime ; whether they be structural modifications or habits. Such a theory is commonly called ' Lamarckism ', after the French biologist J. B. Lamarck (1744–1829), who contended that the effects of use and disuse are inherited. Now many experiments have been performed which purport to demonstrate a transmission of this kind. To do so successfully, it is necessary to use a pure-line, in which the effects of recombination can be excluded, or to make sure that selection is not being practised. The latter is an exceedingly difficult procedure. Satisfactory pure-lines have rarely been used in Lamarckian experiments and, when they have, the results appear to be negative. The suggestion is often made that a process far too slow to be detected by experimental means might none the less be of great importance during the vast periods of time allowable for evolution. The contention as it stands is evidently true, but J. B. S. Haldane has pointed out that it cannot be applied in the situation which we are discussing. Variation, as he says, does not take place continuously but by steps, even if they are extremely small : a fact which seems to be true if it has any material basis at all. Now if some agent causes a

large proportion of the population to vary in each generation, measurable results should be obtained within the course of an ordinary experiment. If, on the other hand, very few change, it can be shown mathematically that the new character cannot spread through the population in the face even of very slight selection. So that such slowly acting causes can do no more than establish characters of practically neutral survival value.

It will by now be perceived that the concept which involves the inheritance of structural characters or habits newly acquired by the individual during its life, is utterly divorced from the realities of heredity and the facts of development. It is not impossible that extraneous agencies may affect the hereditary constitution of the gametes: whether acting indirectly, through the body, or directly—as we know they do in the induction of mutation. But we are asked to believe that, in certain circumstances, whatever causes such a change in habit or structure shall influence the gametes in a very peculiar way. Working through all the complex stages of development, it must modify them to produce that same change which was originally evoked environmentally in the parental body. It is necessary to note that

such effects must persist in successive generations after the agency which causes them has been withdrawn. Otherwise we are simply faced with the well-known fact that a given hereditary constitution produces the same result so long as a particular environment continues. In short, we have no ground for thinking that habits or structures acquired during the life of the parent can be transmitted to the offspring by the hereditary constitution.

It is often found that the evolution of a group of organisms progresses in a ' straight line ' that is to say, they are continually modified in a particular direction. Such an occurrence is called ' orthogenesis '. Thus the evolution of the horses has been consistently marked by certain trends. They have shown a constant tendency to reduce the number of their fingers and toes and to walk on the tips of them. As is well known, the modern horse has only one finger or toe on each foot, together with vestiges of two others preserved as ' splint bones ' which do not show on the surface. At the same time, there has been a progresive complication in the pattern of the teeth along a particular line, adapting them for grinding certain kinds of food. Also the average size of the body has been steadily increased.

Now to say that evolution has proceeded by orthogenesis in a certain group, may be a perfectly correct statement of fact. Unfortunately it has often been made to mean something more: that the group has been impelled along a particular evolutionary course by an 'inward urge'. Used in this sense, orthogenesis is a manifestation of a special type of evolutionary mechanism, in the existence of which we have no justification whatever for believing. As an organism becomes more 'specialized', more closely adapted to its peculiar needs, the types of variation which can possibly be of use to it are restricted. To an 'unspecialized' form, free to adapt itself in any direction which chances to be satisfactory, many variations might be useful which could not possibly be of advantage to a species already definitely committed to one manner of life. Variations in the structure of the teeth which might be useful to a carnivorous animal could not possibly be employed by an herbivorous one. Only those variations can be adopted by a highly modified type which serve to push it along the line which it has begun to follow. It must evolve orthogenetically, or not at all.

It will be perceived that such evolution

leads down a blind alley. The environment may change, but the species may be too highly adapted to be forced along any path but its accustomed one. It cannot adjust itself, and becomes extinct. Yet those variations are constantly selected which adapt the individual to its environment, so that in the end such a high degree of specialization, carrying with it a high probability of extinction, must surely often be attained. Indeed, this is so. The course followed by every evolving line of organisms most usually leads to extinction. Evolution is immensely more often a failure than a success. If orthogenesis is really the result of a determined inward urge, such determination is very ill directed. It leads, by constant repetition of the same mistakes, along a well-worn track to destruction.

As the highly adapted forms are eliminated, so less specialized ones find their opportunity to evolve, generally once more along some groove which will lead them into an irretrievable position. Yet there can be recognized throughout evolution a gradual *progress*. By means exceedingly slow and cruel, there is achieved some real advance. On the whole, each form has to do a little better what has been done before in order to attain temporary

success. The tendency is, after all, an upward one. It has often been maintained that the use of such words as ' progress ' and ' advance ' in evolution is a mere expression of human prejudice : that a jelly-fish is as good an animal (relative to its needs) as a lion ; and how are we to judge between them ? This position is false. There has been throughout evolution a trend which can justly be called progress and, as pointed out by J. S. Huxley, it is comprised in this fact : that living things have, on the average, acquired a greater mastery over their environment.

We have already implied some distinction between minor variation and fundamental evolutionary trends, and this indeed is a reality. The extreme complexity of adaptation may have little or nothing to do with the main course of evolution in a particular group. Minor changes in species may occur rapidly, in a few dozen generations, major evolutionary modifications occupy an immense length of time. The main trend of evolution is less likely to be obscured by minor variation when we study it over long than over short periods.

Such minor variations are to some extent

the result of processes of a rather special kind: in part, of competition between members of the same species. This will lead to an extreme degree of adaptation and to over-specialization, which, as we have seen, is ultimately very dangerous. Sexual selection involving much competition, for example between polygamous males for the females, may tend to increase beyond the optimum for the species the size of the body and the development of organs used in fighting (as horns and antlers). When, as often, these grow disproportionately, a mere increase in size may lead to their extravagant development (pp. 153–4). The largest and most strongly armed individuals then secure most mates and leave most descendants. So too, competition within the species may involve excessive elaboration of organs used in display, to attract the female or to stimulate her in courtship. In short, such competition increases the pressure of selection.

Now the selection pressure to which a species is exposed is a highly important factor in its evolution. Stringent selection will adapt it very closely, often too closely, to its environment. This may give it a great advantage over those forms which have been exposed to less rigorous conditions. It has

long been recognized that the more extreme specializations are to be found in the tropics, where the abundance of life causes great pressure of selection. The species peculiar to islands are generally hopelessly inadequate to compete with forms brought in from the mainland, which have been far more closely selected. So too the indigenous fauna of Australia, long cut off through isolation from the main course of evolution, is failing to maintain a footing in its own environment when opposed by the forms introduced by man.

We must now briefly touch on the idea of species. Even after the principle of evolution was generally recognized, too much importance was attached to the species as a unit. As this error became clear, the tendency has been in the other direction, and to-day it may be that its importance is underestimated. Indeed, it is sometimes said that the species concept is meaningless. This is, frankly, nonsense. The most rational position seems to be an intermediate one between such an extreme—and probably rash—statement and the older view. The latter, in reality, owes not a little to the pre-evolutionary idea that the species represent separate acts of creation. Darwin, in the

greatest of his books, set out in a sense to show how the gulfs between them might be bridged, and that one could evolve into another. At that time a species was regarded as an interbreeding unit, the individuals composing it being fertile with one another and sterile with those of other species. We now know that in a given group every degree may be found from complete fertility, for example among those occurring in the same habitat, to complete sterility between specimens from the extremities of a wide range. Also that two forms which must on all normal grounds be judged as distinct species, may be quite fertile with one another. But these are exceptional instances. Though there exists no definition of the term which is always valid, the concept of species as a group of individuals fertile with one another and sterile with other groups is, on the average, true. Now since species evolve from one another generally (but not always) gradually, they may be connected by intermediate conditions. If all the steps occupied an equal time, we should agree that the species concept is meaningless. But the point which those who hold such a view fail to stress is that when (as usual) the transition is gradual, the timing of it is not uniform.

There is a tendency for the periods spent 'as a species' to be long, and the intermediate stages to be short. Once a species has become divided up into groups between which the free flow of genes is checked by isolation of any kind, evolution along different lines, prevented before, can set in, should different needs arise. This itself leads to a rapid widening of the gulf which initiated it. The relation between species which give rise to one another is not to be thought of as a continuous ramp marked off into arbitrary divisions, as it would be if the species concept were meaningless, but more often as a series of wide steps between which are steep slopes short in comparison with them. (In reality, we must of course think of our steps as branching in many directions.)

We have just picked upon isolation as the chief factor in species formation, and this is undoubtedly correct. If we have a population among which genes can freely be transmitted, its members belong to the same species. Whatever agent isolates them into groups, between which this is no longer true, makes possible their fission into distinct species. This must generally be brought about by geographical barriers, but it may be attained in the same habitat by internal

changes. We have already seen that an allotetraploid plant is as completely isolated from its parent species as if it had been transported to a desert island. So, too, if among the varied characters of polymorphic forms any arise which make it a little more likely that similar types shall mate than dissimilar ones, we have the basis for effective isolation. Thus in many insects mating is ensured by the production of highly characteristic scents. One of these may be elaborated by the female and serves to attract the male, another, produced by the male, stimulates the female in courtship. Any variation in them might produce the effect suggested. For example, the fly normally called *Drosophila pseud-obscura* is really divided into two species. The males will attempt to mate with females belonging to either. If achieved, the wrong pairing is always successful; but it is allowed only in special circumstances. It appears almost certain that the exciting scents of the males are different. How effective such isolation has been in species formation is shown by the fact that the F_1 hybrids are sterile.

This last fact reminds us that even if forms geographically isolated are brought together again, they may have diverged too

far to unite, quite apart from any psychological barriers involved. We have seen that the successful formation of gametes depends upon chromosome pairing. Further, that this is brought about by an attraction between identical units (genes) in homologous chromosomes. If the hereditary constitution of the species has become too distinct through isolation to bring about such attraction, gamete formation cannot be accomplished, and the individuals belong to different species. They are of the same species in which free pairing takes place between homologous chromosomes.

If any barrier to the free passage of genes through a population threatens the specific unity of its members, then every species broken up into a number of pure-lines is in reality composed of so many potential species. This indeed is true. They are potential only, owing to the extreme slowness of their evolution. Diversification is checked because they are almost completely homozygous, and must wait upon mutation to supply their genetic variability. Its usual source, recombination, is closed to them.

In direct contrast to the condition presented by a set of pure-lines, is the type of evolution aptly called ' reticulate ' by J. S.

Huxley. Here groups which have evolved some way individually cross with one another, producing a highly diversified gene-complex, leading to great variability. If the specification has proceeded some distance, chromosome abnormalities will result. Some of these may be preserved through autopolyploidy. Furthermore, occasional doubling will induce fertility among the allopolyploids arising from the more distinct crosses. An inextricable tangle of forms may result, such as to present great difficulties to the systematist. The British roses seem to represent an instance of this kind. It will always be rather an exceptional occurrence but far rarer among animals than plants. In the latter group, the possibility of polyploidy will allow a successful merging of types so distinct that free chromosome pairing no longer occurs in the hybrids between them. In animals, however, this would present an almost complete barrier to such reunion which, if at all, must occur at an earlier stage ; an example of it is undoubtedly provided by man himself. It has become impossible for human evolution to take place through fission. In this instance no doubt exists that a single species only is involved. However, within some of the groups subject to reticu-

spite of them. In this way, among others, selection may be responsible for the spread of undesirable qualities.

It has been pointed out, especially by L. Bolk, that certain conspicuous features which separate man from his near allies, the great apes, are attributable to a retardation of his development. Man indeed resembles in many particulars the embryos of the species to which he is related. Their skull at first resembles his, and comes to differ from it in adult life chiefly by the development of great brow-ridges. In them, the head is at first set at right angles to the body. Its axis later straightens out, but it fails to do so in man. In his relatively hairless condition also, man is embryonic: and, most important, the bones of his brain-case remain separate for a much longer time after birth than in the apes, so that his brain can increase in size for an extended period. Of great significance too is that general delay in mental and physical development which so much prolongs man's baby phase, providing a far greater period for learning. We need not despair of an individual whose capacity develops late: rather, it is the precocious child upon whom we may look with misgiving.

There can be no doubt that genes slowing down development have played a most important part in the production of these crucial features. But they could not have been established had the existence of embryonic competition, such as occurs in the mouse, placed a selective value upon those speeding up early growth. We are indebted to Haldane for recognizing a fact of much significance: were it not for the circumstance that the human species produces on the average but one young at a birth, the evolution of mankind could never have taken place.

The study of heredity has already yielded results of outstanding importance, but the future of the subject may well eclipse the achievements of the past. Up to the present time, research in this science has largely been concerned with the laying down of principles; now they can be increasingly applied. Man has acquired a new and powerful means of improving the plants which he cultivates and the animals he breeds; but he will be able to direct his own future also. The elimination of much physical and mental weakness and, in the end, the control of human evolution may reward the study of heredity if rightly applied.

GLOSSARY

Allelomorphs. The pairs of genes occupying identical loci in homologous chromosomes.

Allopolyploid. A polyploid containing chromosome sets from different species.

Allotetraploid. A hybrid in which the paternal and maternal chromosome sets have doubled in number.

Autosomes. Chromosomes other than the sex-chromosomes.

Back-cross. A mating between a heterozygote and a homozygote.

Cells. The units into which the protoplasm is generally divided.

Chlorophyll. The green colouring matter of plants.

Chloroplasts. Self-perpetuating bodies containing the chlorophyll. They are carried in the cytoplasm.

Chromatin. The deeply staining substance of the nucleus. It is precipitated on to the chromosomes at cell-division.

Chromosome. One of the deeply staining paired bodies which appear in the nucleus preparatory to its division. They are generally constant in number in each species, and carry the genes.

Correlation. The interdependence of different variable characters.

Crossing-over. An interchange of blocks of material between the longitudinally split halves of homologous chromosomes. The genes are transferred in these blocks.

Cross-over value. Those classes in which crossing-over has occurred between a given pair of genes, expressed as a percentage of those in which it has not.

Cytoplasm. Protoplasm other than that contained in the nucleus.

Deletion. The loss of a segment from a chromosome.

Diploid individuals. Those possessing two chromosomes of each type, as in the body-cells.

Dominant character. One which is fully expressed, whether the gene producing it is in the heterozygous or the homozygous state.

Duct. The tube carrying the substance manufactured by a gland to the place where it is required.

Duplication. The addition to a chromosome of a fragment of homologous material.

Fertilization. The fusion of the male and female gametes.

F_1 generation. The first filial generation, being the offspring of a given mating.

F_2 generation. The second filial generation. The grandchildren of a given mating, obtained by interbreeding the F_1 generation.

Gamete. A reproductive cell of either sex.

Gametophyte. The generation of plants which contains the reduced number of chromosomes, and produces the gametes.

Gene. An hereditary factor. The genes are paired (allelomorphs) and are carried in paired (homologous) chromosomes, in which they are situated at definite loci.

Gene-complex. The system produced by all the genes of the organism interacting with one another.

Genetics. The study of heredity and variation.

Genetic variation. Variation due to changes (recombinations or mutations) in the hereditary constitution of the organism.

Genotype. An individual judged by its hereditary constitution.

Germ-cells. Those set apart for the production of gametes.

Glands. Structures which manufacture substances of use to the body.

Haploid individuals. Those possessing one chromosome of each type, as in the gametes.

Heterogametic sex. That carrying unlike sex-chromosomes.

Heteroploid. Individuals possessing an extra chromosome, or a chromosome too few.

Heterozygote. An individual in which the members of a given pair of genes are dissimilar.

Homogametic sex. That carrying similar sex-chromosomes.

Homologous chromosomes. The members of the same chromosome pair, derived respectively from the two parents in bisexually reproducing forms.

Homozygote. An individual in which the members of a given pair of genes are similar.

Linkage. The tendency for genes to segregate together, instead of assorting independently, because they are carried in the same pair of chromosomes.

Melanin. A member of a group of brown and black pigments.

Mimic. As used in this book, a palatable form which resembles a distasteful species for protection.

Mitosis. The process by which the nuclei of cells normally divide. It ensures that each of the daughter nuclei receives a longitudinal half of every chromosome.

Model. The unpalatable form which a mimic copies.

Multiple allelomorphs. The various phases in which the genes at a given locus can exist.

Mutant characters. Those to which a mutant gene gives rise.

Mutant gene. That resulting from a mutation in a stock under investigation.

Mutation. A change in any unit of heredity.

Nucleus. A specialized part of the protoplasm of all normal cells. It carries the chromosomes.

Optimum environment. That best suited to the individual.

Ovary. The structure in which the eggs are formed.

Ovule. The seed rudiments of a plant.

P_1 generation. The parental generation, the individuals of which are mated to produce a given cross.

Phenotype. An individual judged by its appearance.

Placenta. The structure connecting the embryo with the mother, found in most mammals and in some other forms.

Plastids. Self-perpetuating bodies present in the cytoplasm of plants.

Pollen grains. The structures which carry the male gametes of plants.

Polymorphism. The existence of two or more forms of a species in stable equilibrium in the same habitat.

Polyploid. An individual which possesses more than two sets of chromosomes.

Prothallus. The gametophyte generation of a fern.

Protoplasm. The living substance of an organism.

Pure-line. A group of individuals having all their allelomorphs homozygous.

Recessive character. One which is expressed only when the genes producing it are homozygous.

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